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ABSTRACTS OF WORLD MEDICINE

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ABSTRACTS OF WORLD MEDICINE

This journal is planned to provide the reader with a selection of abstracts of the more important articles appearing in medical periodicals published in different parts of the world. Comment by the abstracter, when thought necessary, is inserted between square brackets, usually at the end of an abstract. In some instances only the titles of articles are provided.

After the title of each journal from which an abstract is taken we print the abbreviation given in the *World List of Scientific Periodicals*. The titles of articles from foreign journals are translated into English.

This journal is essentially a guide to work in progress in the world's medical centres. No abstract can be regarded as a substitute for the article abstracted. For complete information the original article must be consulted. Our aim is to give the reader sufficient details in an abstract to enable him to judge whether the original is, for him, worth reading in full.

The abstracts are grouped in broad classifications and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together under the same heading. The specialist will, it is hoped, learn from this journal of work done in other fields as well as in his own. The general practitioner will be able to keep abreast of modern knowledge in the various specialties. The representation in one journal of the several aspects of Medicine will, it is believed, give an integrated picture of the whole, necessary in this age of specialization.

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ABSTRACTS OF WORLD MEDICINE

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Pathology

1065. **The Prothrombin Level in Patients on Dicoumarol Therapy. A Simplified Capillary Technique**
H. B. STEIN and B. V. WALLACE. *South African Medical Journal* [*Sth Afr. med. J.*] **26**, 353–355, April 26, 1952. 13 refs.

A technique is described for estimating the prothrombin level in patients receiving dicoumarol. Thromboplastin extract (prepared from human brain by a standard technique) and capillary blood, 0·02 ml. of each, are mixed on a microscope slide. Mixing is carried out with a clean steel pin, and the end-point is indicated by the adhesion of fibrin to the pin. The results of 200 estimations are compared with those obtained by a laboratory one-stage technique. The results are not statistically analysed farther than to show that the coefficient of correlation was 0·82, but the scatter diagram supports the authors' view that the method should not be used where more adequate laboratory facilities exist.

[When to the inherent disadvantages of such a technique are added the errors that may be introduced by technicians, less skilled than the authors, performing the test in conditions less satisfactory than those obtaining in a scientific laboratory, one is forced to conclude that the value of the technique may be even less than the authors suggest.] *A. Brown*

EXPERIMENTAL PATHOLOGY

1066. **The Basal Substance of the Mesenchyme, and the Diffusion Factors in Infection.** (La substance fondamentale du mésenchyme et les facteurs de diffusion dans l'infection)
F. DURAN-REYNALS. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 1047–1058, April 2, 1952. 4 figs., 34 refs.

The author reviews the present state of our knowledge of the fundamental substance of the mesenchyme and of spreading factors, and gives details of some of his as yet unpublished experiments. He points out that although the main factor in the fundamental substance, hyaluronic acid, is well known, other factors play a part in the resistance of tissues. Similarly although the action of hyaluronidase has been studied, other substances can modify the barrier of the fundamental substance. He cites as examples of factors affecting the permeability of the mesenchyme, adrenaline, salicylic acid, trauma, burns, toxins, and especially hormones. Adrenal cortical extracts suppress the diffusion effect of hyaluronidase, whereas adrenalectomy enhances it. Of the hormones, oestrogen and testosterone increase the mesenchymal barrier, as has been demonstrated in apes before and after puberty. Cortisone and corticotrophin (ACTH) may act directly on the fundamental substance, or indirectly by increasing production of other hormones.

Apart from affecting the amount of hyaluronic acid, these factors may cause polymerization or change of chemical structure to take place. Experiments *in vitro* with dinitrated and sulphonated hyaluronic acid show that these derivatives are more active than hyaluronic acid itself. The author has also shown that certain substances produced by heating hyaluronic acid and by the action of hyaluronidase on the acid inhibit the growth of vaccinia virus. He suggests that the fundamental substance of the mesenchyme may also play a part in natural immunity, as it has been found that in an inbred strain of rabbits the degree of susceptibility to tuberculosis bears a direct relationship to the permeability of the tissues.

[This article contains many descriptions of experiments which cannot be abstracted and should be read in full by workers interested in this subject, of which it provides an excellent review.] *R. F. Jennison*

1067. **The Response of the Renal Circulation of the Rabbit to Adrenaline. An Inquiry into the "Trueta" Shunt**
H. J. BARRIE, G. W. CATES, and E. A. MCCULLOCH. *British Journal of Surgery* [*Brit. J. Surg.*] **39**, 465–469, March, 1952. 8 figs., 6 refs.

Trueta and others have stated that the juxtamedullary glomeruli have a blood circulation that is functionally independent of that of the outer part of the cortex. In the experiments described in this paper from the University of Toronto, adrenaline in doses of 2·0 to 0·05 mg. was given intravenously to pentobarbitone-anaesthetized rabbits, and at intervals thereafter indian ink was injected at pressures of 160 and 80 mm. Hg into the aorta. After this injection the renal pelvis was clamped, the kidney removed and fixed in 10% formalin for 24 hours, and serial sections 200 to 300 μ in thickness were cut. Control animals were studied. The high-pressure injections accentuated changes in the larger vessels and low-pressure injections accentuated changes in small vessels.

At both high and low pressures at certain stages after the injection of adrenaline the juxtamedullary region contained ink while the cortex was pale. This was believed to be due to reflux of ink from the renal sinus, where the circulation was not affected. An additional

reason for this picture in the low-pressure injection studies was a relaxation of vessels up to and just beyond the glomeruli in all areas, the cortical efferents being constricted while the juxtamedullary efferents were open up to the termination of the long efferents. There was no evidence of medullary circulation. It was concluded that no independent circulation through juxtamedullary nephrons could be shown. *G. M. Bull*

1068. **Atherosclerosis. An *in vitro* Study of the Pathogenesis of Atherosclerosis**
S. M. EVANS, H. K. IHRIG, J. A. MEANS, W. ZEIT, and E. R. HAUSHALTER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **22**, 354–363, April, 1952. 2 figs., 17 refs.

This work is reported from Marquette Medical School, Milwaukee, Wisconsin. Believing that in atherosclerosis the lipoids are deposited in the vessel wall during the passage of plasma from the main lumen to the adventitial vessels, the authors have attempted to produce atheroma *in vitro*. For this purpose a number of identical, cylindrical, stainless steel chambers each holding about 30 ml. of blood were constructed. On the floor of these chambers was a hole 7 mm. in diameter over which a strip of aorta was secured. After the blood had been added a rubber diaphragm was placed over the top of the chamber, which was then connected to an electronically controlled pressure system, in which the air pressure was raised from 0 to 300 mm. Hg 80 times a minute. The plasma which was forced through the aorta was returned to the chamber through a ball valve. The chambers were maintained at 37° C. by a water bath. Strips of fresh aorta obtained at necropsy from one young human subject were attached to 12 chambers each containing a sample of blood from a different source and 30 units of penicillin. All the chambers were connected to the pressure system and thus received identical pulsations, usually for 72 hours.

Of the experiments with blood from patients with atherosclerosis an "atheroma" was produced in 75%. The atheromata showed a remarkable resemblance to naturally occurring aortic lesions in man. With blood from 22 patients without obvious evidence of atherosclerosis 82% of the results were negative, while none was definitely positive. *Peter Harvey*

CHEMICAL PATHOLOGY

1069. **Methionine Tolerance as a Test of Liver Function.** (Methioninbelastung als Leberfunktionstest)
K. SCHREIER and H. SCHONSEE. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] 77, 418–420, April 4, 1952. 2 figs., 12 refs.

The introduction of yet another liver function test seems to be justified only if it tests some partial function which could not be examined by previously known tests, or if its simplicity enables it to be performed outside the well-equipped laboratory. The latter is the case, in the authors' opinion, with their methionine-tolerance test, which originates from the University Clinic for Children, Heidelberg. They found that in cases of liver damage the methionine level in the serum showed a marked elevation after oral administration; the urinary excretion of this amino-acid was also greatly increased, showing, in the authors' opinion, that the damaged liver cells find it difficult to metabolize methionine. The methionine levels remained elevated for some time.

As the estimation of methionine in the serum is difficult, the authors recommend its determination in the urine. To children they give 0·2 g. of methionine per kg. body weight, and to adults a standard dose of 10 g. During the previous day all medicaments are stopped; the methionine is given in tea the next morning, after a specimen of urine has been collected for estimation of the zero level, and specimens are collected at 3-hour intervals for the next 24 hours. Of each specimen 0·5 ml. is placed in a separate test-tube, made up with distilled water to 5 ml., and well shaken. To this, 1 ml. of 5N sodium hydroxide and 0·1 ml. of a 10% solution of sodium nitroprusside are added (the latter has to be prepared freshly each day) and left for 10 minutes; then 2 ml. of a 3% solution of amino-acetic acid is added and left for another 10 minutes. Finally, 2 ml. of 85% orthophosphoric acid is added and the tube vigorously shaken for 1 or 2 minutes and left standing for a further 10 minutes. The result can then be read in a Pulfrich photometer, using filter F53, or if more convenient an electric colorimeter may be used, or a simple comparator. A standard curve can easily be constructed with known amounts of methionine.

For the purpose of observing the normal rate and range of elimination, 48 normal children between the ages of 6 and 15 years and 10 adults were subjected to the test. The results showed that in the adults 50 to 60% of the total elimination was completed within 6 hours, whereas the children excreted roughly 75% within 6 hours, and the whole amount within 9 hours. It was also shown that the average total elimination in a healthy adult ranges between 11·5 and 13% of the dose of methionine administered, and in children the average is 9·3%. Excretion amounts of 15 to 19% are high values, and above 19% definitely pathological in adults, while in children anything above 15% is considered to be abnormal. *E. Forrai*

1070. **The Benzidine Test for Occult Blood in Faeces**
C. D. NEEDHAM and R. G. SIMPSON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **21**, 123–133, April, 1952. 2 figs., 38 refs.

The authors describe a modification of the Gregersen benzidine test for occult blood in faeces. A powder consisting of a finely divided mixture of benzidine hydrochloride (25 mg.) and barium peroxide (200 mg.) is shaken up with 5 ml. of glacial acetic acid to give the test solution. (The authors state that if the powder is wrapped in wax paper it will retain its potency for more than a year.) Either the examining finger of a rectal glove or an orange stick dipped in a faecal specimen is smeared on white filter paper and a little of the test solution poured over the smear. The reactions are graded

as follows: positive, a deep blue colour appearing within 15 seconds; weakly positive, a greenish-blue colour within 30 seconds; negative, no colour within 30 seconds.

When dilutions of blood were mixed with blood-negative stools the test was sensitive to dilutions of 1 in 500 of blood, but it required 3 to 5 ml. of blood given by a Ryle tube into the stomach for a positive result to be obtained in the stools of 17 patients. The stools of 3 subjects who had been taking iron ammonium citrate, 60 gr. (4 g.) daily, and 2 who had had ferrous sulphate, 9 to 18 gr. (0·6 to 1·2 g.) daily, for at least 10 days before the experiment did not give a positive reaction. The only foodstuffs which, when eaten in the customary quantities, had any effect on the benzidine reaction were black pudding and liver. The stools of 187 out-patients who had eaten meat on the 3 previous days were examined, and in all but 20 the examination was completed. In the absence of a proved source of bleeding 6 patients gave a weakly positive reaction and 7 a positive reaction, and of this latter group 5 had eaten black pudding or liver the previous day. The medical records of 603 out-patients whose stools had been tested during the previous 2 years by this modified technique were examined, and of the 149 positive reactions obtained in these cases only 11 appeared to have no clinical significance.

[The technique is simple and its sensitivity is such that dietary restriction before the test is performed does not appear to be necessary. Although the number of false-positive reactions is reduced, the relative insensitivity of the method compared with the usual benzidine test makes the occurrence of false-negative reactions much more likely.] *M. J. H. Smith*

MORBID ANATOMY AND CYTOLOGY

1071. **A Study of Cerebral Lesions due to the Anoxia Resulting from Respiratory Paralysis.** (Étude des lésions cérébrales de l'anoxie au cours des paralysies respiratoires)

T. ALAJOUANINE, I. BERTRAND, P. CASTAIGNE, J. GRUNER, and J. PECKER. *Revue Neurologique* [*Rev. neurol.*] **64**, 3–24, 1952. 7 figs., 42 refs.

The authors made a systematic neurohistological study of the central nervous system between the cervical cord and the cerebral cortex in 12 cases of poliomyelitis, one of polyneuritis, and one of Landry's ascending paralysis, in each of which death had been due to respiratory failure. In 10 of the cases the patient had been treated in a respirator for periods ranging from 2 hours to 105 days.

In addition to the typical inflammatory changes of poliomyelitis present below the level of the mesencephalon, in 8 of the 12 cases degenerative changes were found in the cortex, hippocampus, and basal nuclei. These the authors attribute to anoxia, as they were similar in appearance and distribution to those due to anoxia from other causes such as exposure to high altitudes, overdosage of anaesthetics, cardiac failure, and congenital heart disease. Similar degenerative changes were also found in the single case of Landry's paralysis. In only 4 of these cases had there been clinical signs of cerebral anoxia—mental confusion, partial loss of consciousness, and in one case clonic spasms confined to the muscles of the face. The authors conclude, however, that there is sufficient clinical and pathological evidence of the existence of an anoxic encephalopathy in cases of this type to justify further study with a view to establishing its physiological basis.

[Some fine photomicrographs of the lesions described are reproduced.] *L. Michaelis*

1072. **The Pathology of Pleonosteosis.** (Zur Pathologie der Pleonosteose (Léri))

A. MATERNA. *Beiträge zur pathologischen Anatomie und zur allgemeinen Pathologie* [*Beitr. path. Anat.*] **112**, 112–136, 1952. 15 figs., 36 refs.

In 1922 Léri described a family in which 3 individuals (the father and 2 children) were affected with a condition manifested by dwarfism, irregular thickening of limb bones, and flexional deformities of the fingers. He gave the name *pléonostéose* (superfluous ossification) to the syndrome, which is now usually grouped with two other rare familial conditions, the Morquio–Brailsford syndrome, and the Pfaundler–Hurler syndrome (gargoylism), the entire group being known as the endochondral dysostoses or osteochondrodystrophies. The skeletal changes in the 3 types have certain similarities, but pleonosteosis shows a dominant mode of inheritance, while the other two are recessive. [British and American literature contains little reference to pleonosteosis; one article, however, by Watson-Jones (*J. Bone Jt Surg.*, 1949, **31B**, 560) directs attention to the soft-tissue changes present in the condition, and gives a bibliography, mainly French, up to 1949.]

So far, descriptions of the osteochondrodystrophies have dealt chiefly with the clinical pattern and the observed radiographic changes, but little has been said concerning their underlying pathology or of the mechanism by which the genetic abnormality affects the developing skeleton. The present paper makes a start in this direction by putting on record the gross and microscopic bone changes found post mortem in a case of pleonosteosis studied in Czechoslovakia during the period of German occupation. Two brothers and their father were affected, but details were available for only one of the brothers, who died at the age of 39 with infective hepatitis and old rheumatic carditis. His skeleton showed what are regarded as the characteristic changes of the condition. He was of short stature, with a conspicuously short neck; the large skull had a thickened vault and there was exaggerated growth of the facial bones. The spine showed thoracic kyphosis and lumbar lordosis, and the intervertebral disks were " ballooned ", giving the vertebral bodies a narrowed biconcave outline; one thoracic vertebra was grossly collapsed anteriorly.

Histological study showed that an excess of irregularly arranged trabeculae of the medullary spongiosa, and not thickening of the cortical bone, was responsible for the irregular bone structure. There was a general lack of osteoblastic and osteoclastic activity, and numerous small

fractures were present, particularly in the skull, the vertebrae, and at the ends of the long bones. In the vertebrae bony collapse with cyst formation was frequent. There was also absence of haematopoietic marrow, and numerous Schmorl's nodes were present. Many of the bones contained areas of cartilage which were thought to be either persistent developmental foci or areas of callus consequent on fracture and bony collapse. A severe degree of osteo-arthritis was present in the hip-joints, and was regarded as secondary to the local alterations in bony structure.

The author regards the pathogenesis of pleonosteosis as not yet elucidated. He notes a similarity of the histological changes to those of certain other bone diseases, but attributes this to the limited potentialities of reaction of the skeletal tissues rather than to essential affiliations of the disease process. [It is unfortunate, as the author points out, that clinical radiographs of the affected bones could not be reproduced, but this material was destroyed in the war.] *H. A. Sissons*

1073. **Evidence that Aschoff Bodies of Rheumatic Myocarditis Develop from Injured Myofibers**

G. E. MURPHY. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 319–331, March 1, 1952. 33 refs.

The theory advanced in this paper is that myocardial Aschoff bodies result from focal injury to cardiac myofibres, and that certain elements in these lesions are directly derived from the muscle fibre or its ensheathing sarcolemma. The material studied was taken from 12 patients aged from one to 19 years who died during a first or second attack of rheumatic fever, and from 3 rabbits, 5 to 22 months old. The rabbits were examined 8 to 15 days after the last of a series of streptococcal injections (as described by Murphy and Swift in previous papers in this series (*J. exp. Med.*, 1949, **89**, 687 and 1950, **91**, 485; *Abstracts of World Medicine*, 1950, **7**, 223 and **8**, 598)). No micro-organisms were seen (in sections specially stained for the purpose) in any of the hearts examined, nor, in the rabbits, were post-mortem blood cultures positive.

By a series of 32 photomicrographs showing comparable lesions in rabbit and human hearts, the author demonstrates an apparent sequence, starting with an injured muscle fibre surrounded by basophilic and multinucleated syncytial cell masses, " probably myogenic ", and progressing to the classical Aschoff nodule. In the rabbit material the earliest lesions appeared in the myofibrils, which became necrotic and, when stained with haematoxylin and eosin, somewhat resembled what has been called " fibrinoid necrosis ". They also became surrounded with syncytial and basophilic multinucleated cell masses originating from beneath the sarcolemma. In some instances, in both rabbit and human, grossly necrotic areas of cardiac papillary muscle might be seen. Human skeletal muscle in one case also showed somewhat similar degenerative lesions. It is not yet clear what mechanism is responsible for this damage to the myofibrils. In the lesions illustrated there was no fibrinoid change in or between collagen fibres (as shown in previous communications), and the author considers that this is not an essential or primary change in the development of the Aschoff body.

The very close similarity between the lesions developed in a few of the rabbits subjected to repeated focal infections and the lesion in human beings supports the author's view that at least one factor in the pathogenesis of rheumatic fever is repeated infection with Group A β-haemolytic streptococci of differing serological types. *E. G. L. Bywaters*

1074. **Renal Papillary Necrosis**

A. KNUTSEN, E. R. JENNINGS, O. A. BRINES, and A. AXELROD. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **22**, 327–336, April, 1952. 6 figs., 19 refs.

Renal papillary necrosis has only recently become generally recognized as a distinct pathological entity occurring almost exclusively in patients with diabetes mellitus or with chronic obstruction of the urinary tract. The authors report 16 cases, collected during a period of 38 months (August, 1947, to October, 1950), the diagnosis having been made at necropsy in 14, on examination of a kidney removed for a unilateral renal infection in one, and on histological examination of a necrotic papilla removed cystoscopically in one. Of 11 patients with diabetes, 8 showed evidence of urinary tract infection. In 4 other patients there was urinary tract obstruction, with or without infection, and the remaining patient had far-advanced portal cirrhosis. There was a distant focus of infection in 8 of the patients (7 diabetics).

Three different clinical patterns were observed: an acute clinical course with severe renal or systemic infection, progressive azotaemia, coma, and death, 6 patients (5 diabetics); a subacute course with gradual but progressive azotaemia, 8 patients (5 diabetics); renal calculus, which was apparently unilateral and self-limited, 2 patients.

Macroscopically, the cut surface of the kidney showed pale yellow, sharply demarcated lesions involving the tips of the papillae and extending into the pyramids for varying distances. The histological appearance was that of sharply circumscribed areas of coagulative necrosis surrounded by a hyperaemic zone of reaction. No general type of glomerular lesion was present, and neither the proximal nor the distal convoluted tubules were altered, except for the direct damage resulting from infection. Thrombosis in the blood vessels was found in one case only, but thickening and hyalinization of the blood-vessel walls were often seen. Some degree of arteriosclerosis of the arcuate arteries was observed in 9 cases, the smaller arteries being sclerotic in 10. Cortical hyperaemia was encountered in one patient only, while medullary ischaemia, apart from the necrotic zones, was not conspicuous.

The gross and histological changes in the kidneys did not support the hypothesis of a reverse Trueta shunt in the development of the lesion. Acquired renal ischaemia from vascular disease appeared to be the most important predisposing factor, with the normal relative ischaemia of the renal papilla localizing the lesion to its characteristic site. *A. Ackroyd*

Bacteriology

1075. **Toxicity of Elemental Sulfur for Brucellae**
V. T. SCHUHARDT, L. J. RODE, G. OGLESBY, and C. E. LANKFORD. *Journal of Bacteriology* [*J. Bact.*] **63**, 123–128, Jan., 1952. 2 figs., 18 refs.

In previous reports the authors described the toxicity of autoclaved cystine for brucellae (*J. Bact.*, 1950, **57**, 1 and **58**, 665). Further work has now been carried out to identify the toxic agent. By repeated adsorptions of solutions of autoclaved cystine with " norit " (activated charcoal), followed by elution with pyridine, pure elemental sulphur was obtained. Although it seemed unlikely that sulphur was toxic, experiments were carried out with colloidal dispersions of sulphur. It proved to be toxic in as low a concentration as 0·06 μg. per ml., the actual amount varying with the composition of the basal medium. The toxic effect was reduced by autoclaving the sulphur in the presence of the medium used. In comparative studies the toxicity of colloidal sulphur was found to be practically identical with that of autoclaved cystine and tryptase. Attempts were made to identify the steps by which autoclaved cystine yields free sulphur, and a possible mechanism for the degradation is outlined. *R. F. Jennison*

1076. **Oxalic Acid and Acid–Iron-Peroxide in the Routine Culture of Tubercle Bacilli from Sputum**
C. H. COLLINS. *Tubercle* [*Tubercle, Lond.*] **33**, 149–151, May, 1952. 6 refs.

A comparison was made of the Jungman acid–iron-peroxide and the oxalic acid methods of pre-treatment of sputum prior to culture for tubercle bacilli. The results were examined statistically. The oxalic acid method was in several ways superior to that of Jungman. Saline washing of sediments from both these methods of pre-treatment was not considered to be entirely satisfactory. Eight weeks' incubation of cultures is recommended, particularly with material from streptomycin-treated cases. —[Author's summary.]

1077. **Resistance of *Mycobacterium tuberculosis* to Streptomycin.** (Résistance des bacilles tuberculeux à la streptomycine)
H. BEEUWKES and H. VOS. *Poumon* [*Poumon*] **8**, 25–39, Jan., 1952. 17 refs.

In determining the sensitivity of *Mycobacterium tuberculosis* to streptomycin the authors employ the following technique: 6 ml. of sputum is shaken up with 12 ml. of a 4% solution of caustic soda for 15 minutes, centrifuged, and three drops of the emulsion sown with a Pasteur pipette in tubes containing respectively Lowenstein medium with 2% glycerin, a modification of Lowenstein medium, and three similar tubes containing 1, 10, and 1,000 μg. of streptomycin per ml. The tubes are examined weekly; all manipulations are done in an enclosed space in which ultraviolet irradiation is used to sterilize the air. At regular intervals the sensitivity of the cultures to streptomycin is tested. By this procedure it was shown that 17·4% of subcultures developed variation in their resistance to streptomycin; of these, 80% showed an increased resistance and 20% an increased sensitivity. This phenomenon was examined in organisms from sputum in 175 cases of active tuberculosis treated with 1·0 to 1·8 g. of streptomycin daily. Resistance may develop after only 2 weeks' treatment, and the number of resistant strains increases with the duration of treatment. Once resistance has developed in a subculture *in vitro* it is a permanent characteristic of that strain, but *in vivo* this does not hold. In 27 out of 66 patients harbouring resistant strains sensitivity returned after a period of continued treatment.

The development of drug-resistant strains is correlated with the site of infection. It occurred in 45% of 130 cases of pulmonary tuberculosis with cavitation, and only in 18% of cases of non-pulmonary disease. Resistance may vary widely in organisms obtained from different sites in the same patient; for example, details are given of a case of pulmonary tuberculosis complicated by tuberculous meningitis, in which streptomycin-resistant organisms were found in the sputum and streptomycin-sensitive organisms in the cerebrospinal fluid. Cavitation always accompanied a high degree of resistance in this series, and the authors state that the development of resistance to streptomycin in a concentration of 1 mg. per ml. is indicative of the presence of a cavity. Nevertheless the presence of resistant strains is not a contra-indication to treatment with streptomycin, which may benefit lesions at other sites such as the larynx, nor is it a contraindication to operative procedures such as resection. The authors are strongly against treatment by a number of short courses and prefer one prolonged course, as after an interval resistance frequently develops to a high degree in previously sensitive organisms. The recommended course of treatment is 1 g. of streptomycin per day in two doses for 6 weeks, combined with PAS; the latter may be continued after the streptomycin injections are complete. *James D. P. Graham*

1078. **The Influence of Vitamins on the Growth of Dermatophytes *in vitro*.** (Sur l'influence de certains facteurs vitaminiques dans le développement *in vitro* de quelques dermatophytes)
X. VILANOVA and M. CASANOVAS. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **79**, 25–29, Jan.–Feb., 1952.

Details are given of an attempt to overcome some practical difficulties in the routine laboratory culture of fungi by using media enriched with various vitamins and other accessory factors. *para*-Aminobenzoic acid was found to be a strong inhibitor of growth, whereas pyridoxine, aneurin, calcium pantothenate, and particularly *meso*-inositol (0·6%) had a definite activating action.
James Marshall

Pharmacology

1079. **The Effect on the Heart of Certain Sympathicomimetic Drugs with Peripheral Vasodilator Action.** (Zur Herzwirkung einiger Sympathicomimetica mit peripher gefässerweiternder Wirkung)
K. GOLLWITZER-MEIER and H. JUNGMANN. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **214**, 349–357, 1952. 3 figs., 10 refs.

This paper from the University of Hamburg records the effects on the denervated heart in the heart–lung preparation of the dog of two sympathicomimetic amines, phenylbutylnoradrenaline and phenyl*iso*butylnorsuprifen, which cause dilatation of peripheral vessels and have been used in the treatment of peripheral vascular diseases. These effects are similar to those of adrenaline. Diastolic volume and right auricular pressure are reduced; contractility, frequency of beat, oxygen uptake, and minute volume are increased. There is coronary vasodilatation and an improved blood supply to the heart muscle. These effects, except for coronary dilatation, become less or disappear on repeated injection, but the drugs are no less effective if they are injected during a continuous infusion of adrenaline. These results indicate that there is no clinical contraindication, on the grounds of untoward cardiac effects, to the use of these drugs in suitable peripheral vascular diseases. Their associated action on the heart may be advantageous.
Derek R. Wood

1080. **The Effect of Volatile 1-*cyclo*Hexyl-2-methylaminopropane (" Benzedrex " Inhaler) on Patients with Coronary Arteriosclerosis**
J. B. BURNETT and S. M. GUNDERSEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 449–450, March 20, 1952. 7 refs.

The drug 1-*cyclo*hexyl-2-methylaminopropane is an analogue of amphetamine, but has only half its pressor potency and is less active as a stimulant of the central nervous system; on the nasal mucosa, however, its action is nearly the same. It was given by inhalation in doses calculated to be about three times the normal therapeutic dose to 20 patients suffering from attacks of angina pectoris; there were no undesirable reactions. The electrocardiogram showed no abnormalities, except for a few ectopic beats in 2 patients. *V. J. Woolley*

1081. **Distribution and Fate of Anaesthetic Drugs**
C. A. KEELE. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **45**, 245–248, May, 1952. 21 refs.

Procaine is rapidly hydrolysed to its components *p*-aminobenzoic acid (PABA) and diethylamino-ethanol (DEAE) by procaine esterase, an enzyme which occurs in plasma and in the liver. The enzyme in human plasma has been shown *in vitro* (Brodie *et al.*) to be capable of destroying 5 mg. of procaine per litre in about 5 minutes, and infusions of procaine *in vivo* produce only low plasma concentrations. Experiments have shown that this is mainly due to the rapid destruction of the drug; within 24 hours 90% of the PABA and 33% of the DEAE appear in the urine. Most of the PABA is conjugated with glycine to form *p*-aminohippuric acid, some combines with glucuronic acid, and small amounts occur in the free or acetylated forms. The products of metabolism of DEAE are not known. Procaine is so rapidly destroyed that it is not possible to determine its concentration in various organs after injection.

The barbiturates, however, are more stable and their distribution in the tissues is more easily studied. The injection of the median hypnotic doses of thiopentone and hexobarbitone in mice causes sleep in 1 to 2 minutes, whereas pentobarbitone and barbitone take 5 and 22 minutes respectively. Equilibrium between blood and brain is established for thiopentone 1 minute after injection. The oil/water coefficient for thiopentone is about 4·7, whereas that for barbitone is 0·214. The brain takes up barbitone more slowly than it does " hexethal ", and experiments with barbitone containing the isotope ^{15}N provide no evidence of selective concentration of the drug in any particular region of the brain. After the intravenous injection of thiopentone the plasma level falls rapidly at first and then more slowly. This is accounted for by speedy distribution of the drug throughout the tissues, most of it being taken up by the fat. It is subsequently released from the fat and detoxicated relatively slowly by oxidation. Up to 90% of a dose of barbitone is excreted unchanged in the urine, but only 25% of a dose of phenobarbitone is excreted in this way, the remainder being detoxicated. The short-acting barbiturates are almost completely destroyed by oxidation of the side-chain (in the liver certainly, and possibly in the kidney and brain).

D-Tubocurarine has a negligible solubility in lipids and does not easily penetrate the cells. It does not cross the placenta, nor does it penetrate central nervous tissue in the usual doses. In mice 60% of tubocurarine is inactivated within 4 hours, perhaps largely in striated muscle. Decamethonium and hexamethonium have a low lipoid solubility and are distributed in the plasma and interstitial fluid. Decamethonium does not cross the placenta. The methonium compounds are not metabolized and are excreted almost entirely in the urine. The drugs pass out via the glomeruli, and if the blood pressure falls below 50 mm. Hg, glomerular filtration stops and the excretion of a drug such as hexamethonium ceases. *P. A. Nasmyth*

1082. **A New Ganglion-blocking Agent. Trial of " Ciba 9295 " in Man**
A. G. BAIKIE and J. R. SMITH. *Lancet* [*Lancet*] **1**, 1144–1145, June 7, 1952. 4 figs.

Chemotherapy

1083. **On the Lasting Protective Effect of Hydrazine Derivatives of *iso*Nicotinic Acid in the Experimental Tuberculosis Infection of Mice**

E. GRUNBERG, B. LEIWANT, I. L. D'ASCENSIO, and R. J. SCHNITZER. *Diseases of the Chest* [*Dis. Chest*] **21**, 369–377, April, 1952. 9 refs.

Mice infected by the intravenous or intranasal route with H37Rv strain of *Mycobacterium tuberculosis* were treated for 21 days with antituberculous drugs and then observed during a further period of 21 days without the administration of any drug. At the end of that time all survivors were killed and examined. An animal was considered as " protected " if there was complete absence of gross lesions in the lungs or when cultures taken from the lungs did not show any growth of tubercle bacilli.

Streptomycin, PAS, " tibione ", nicotinaldehyde, thiacetazone, and *iso*nicotinaldehyde thiosemicarbazone failed to produce a lasting protection, even when given in high doses. In the intravenously-infected group *iso*nicotinic acid hydrazide, in doses of 50 mg. per kg. body weight daily, and its *iso*propyl derivative, 25 mg. per kg. daily, gave lasting protection to approximately 50% of the animals, and in smaller doses lengthened the life span and reduced the severity of the pulmonary lesions. In the intranasally-infected group *iso*nicotinic acid hydrazide and its *iso*propyl derivative protected the majority of the animals when given in a dose as low as 12·5 mg. per kg. daily.

The authors suggest that these two compounds have a direct effect on the viability of the tubercle bacillus, but that further, more sensitive, experiments are necessary to decide whether the tubercle bacilli are actually killed.

G. M. Little

ANTIBIOTICS

1084. **Further Experiences with Local and Systemic Bacitracin in the Treatment of Various Surgical and Neurosurgical Infections and Certain Related Medical Infections**

F. L. MELENEY, B. A. JOHNSON, and P. TENG. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **94**, 401–425, April, 1952. 6 figs., 48 refs.

For the local treatment of carbuncles or abscesses the authors recommend the use of a bacitracin solution containing 1,000 units per ml. mixed with an equal volume of 2% procaine. The normal dose is 0·1 to 0·3 ml., but a large carbuncle may require 0·5 or even 1·0 ml. The injection is made into the centre or round the circumference of the carbuncle. In many cases abscess cavities can be treated by two or three aspirations followed by injection of this solution. Bacitracin can also be applied to surface wounds in a " carbowax " base containing 500 units per gramme of ointment. For neurological infections 5 to 10 ml. of bacitracin solution containing 500 to 1,000 units per ml. may be instilled intrathecally. The authors briefly describe 4 cases in which bacitracin was applied locally.

The antibiotic was given systemically in over 160 cases, with or without supplementary treatment. Of the 131 cases of established infection, 97 had failed to respond to treatment with other antibiotics, but when bacitracin was given favourable results were obtained in 72%. The results were good in 91% of patients who had had no previous treatment. The recommended dose is 200 to 400 units per kg. body weight a day. The solution should be made up in normal saline containing 2% procaine so as to reach a concentration of 10,000 units per ml. It should be given intramuscularly every 8 hours; it may also be administered intravenously in saline by slow infusion.

Evidence of nephrotoxicity was absent or mild in 68% of cases, moderate or transient in 30%, and disturbing in 2%. There is no fear of this complication with doses up to 50,000 units a day.

A. W. H. Foxell

1085. **The Effect on Experimental Tuberculosis and Other Infections of a Micrococcin–Triton Solution**

N. G. HEATLEY, J. L. GOWANS, H. W. FLOREY, and A. G. SANDERS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **33**, 105–122, April, 1952. 10 figs., 13 refs.

Micrococcin is an almost insoluble antibiotic with mainly bacteriostatic action, but it can be dissolved in solutions of bile salts, and in various synthetic detergents gives colloidal preparations. In the present work, colloidal suspensions of 5 mg. per ml. were made up in " triton WR–1339 " (10 mg. per ml.) which is a non-toxic detergent of the non-ionic type described as an " alkyl aryl polyether alcohol ". Triton has no action upon the growth of bacteria but it considerably diminishes the antibacterial action of micrococcin. Small intravenous doses of micrococcin–triton solution are non-toxic; large ones damage the glomeruli of the kidney. The distribution of the micrococcin can be studied histologically because it is strongly fluorescent in ultraviolet light. After intravenous injection of the mixture much of it is first accumulated in the lungs, but after 2 or 3 days it is distributed in the cells of the reticulo-endothelial system (especially in the spleen and liver) as is usual for fine particles injected into the blood. It does not penetrate significantly into tubercles or into the tissue fluids. Micrococcin can still be detected in the liver and spleen of animals after 5 months. The micrococcin–triton suspension has some protective action for mice infected with *Streptococcus pyogenes*, but it does not kill all the streptococci and when the treatment ceases many of the mice die. It has no significant protective or curative action in guinea-pigs infected with tuberculosis,

thus being inferior to particulate preparations of micrococcin.

[Although this work has not yielded results of practical application, it raises many points of interest for those concerned in the attempt to control tuberculosis by chemotherapy.] *F. Hawking*

1086. **Aplastic Anemia following Prolonged Administration of Chloramphenicol. A Report of Two Cases, one a Fatality**

L. E. WILSON, M. S. HARRIS, H. H. HENSTELL, O. O. WITHERBEE, and J. KAHN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **149**, 231–234, May 17, 1952. 7 refs.

In an investigation [to be reported in full elsewhere] of the effects of chloramphenicol in the bacteriostatic control of chronic bronchopulmonary suppuration, 62 patients, whose ages ranged from one year to 72 years, were given the drug over periods varying from one month to 14 months. The dosage was 1 g. twice or three times weekly; in a few instances it was given daily.

Two patients developed aplastic anaemia after receiving the drug for approximately 7 months and 5½ months respectively. First signs of the anaemia appeared after a total of 52 g. and 56 g. respectively had been administered. One of the patients died.

Reference is made to five other papers in the literature reporting haematopoietic changes due to chloramphenicol. The authors recommend that blood counts should be carried out twice weekly in all cases in which chloramphenicol is being given for prolonged periods.

A. W. H. Foxell

1087. **The Use of Chloramphenicol as a Topical Application.** (L'impiego topico del cloramfenicolo)

G. PAULETTA. *Giornale Italiano di Dermatologia e Sifilologia* [*G. ital. Derm. Sif.*] **93**, 67–78, Jan.–Feb., 1952. 1 fig., 19 refs.

The author has shown chloramphenicol to be suitable for topical application; his findings were as follows: (1) The antibiotic was effective in controlling 95% of infections with streptococci, 98% of infections with staphylococci, 75% with *Proteus*, 72% with *Pseudomonas*, and 1·86% with coli-aerogenes. No significant degree of resistance to this antibiotic was developed by any of these organisms in a large series of trials *in vitro*. (2) Its activity was not reduced by pus or exudates. (3) The general and local toxicity was very slight; 2·5% aqueous solutions or suspensions of 10 to 40% in gum acacia were applied to the cornea of rabbits or injected subcutaneously without irritant effects. (4) When attempts were made to sensitize guinea-pigs by giving repeated injections of saline, of chloramphenicol, or of 2:4-dinitrochlorobenzene to groups of animals and then applying solutions to the shaved skin, no sensitization to saline or chloramphenicol could be demonstrated. (5) Chloramphenicol readily penetrated intact skin of the guinea-pig from a suitable base, and was subsequently found in the blood and urine. The antibiotic was made up in various ointment bases and applied to the skin of guinea-pigs which had been depilated with barium sulphate and washed. A fixed area was anointed and a plastic bandage applied. After a given time the animal was anaesthetized and urine and blood samples were withdrawn, the residual cream being also removed from the area of skin. The antibiotic content of these samples was assayed by several techniques. (6) Chloramphenicol did not inhibit wound healing or scar formation and might accelerate it. (7) The antibiotic was most effective in eradicating infection. Two groups of guinea-pigs were inoculated intradermally with staphylococci, one group being treated with chloramphenicol ointment. At varying periods animals were killed and the numbers of live organisms in the skin were estimated by homogenizing the specimen and plating out.

James D. P. Graham

1088. **Penicillin and Chloramphenicol in the Treatment of Infections due to *Proteus* Organisms**

B. A. WAISBREN and C. CARR. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 418–421, April, 1952. 15 refs.

An investigation was carried out at the University of Minnesota Medical School and the Minneapolis General Hospital into the relation between the clinical response of *Proteus* infections of the urinary tract to various antibiotics and the sensitivity of the same strains *in vitro*. In 20 of the 23 cases studied the organism was isolated before treatment: 3 strains were resistant to chloramphenicol, 6 to penicillin, and only one to a combination of chloramphenicol and penicillin *in vitro*. Clinically, 5 out of 13 patients treated with chloramphenicol (0·75 g. 4 times a day for 3 days) responded satisfactorily, and 3 out of 15 treated with penicillin (300,000 units twice a day for 3 days) responded well. Six patients were treated with a combination of penicillin and chloramphenicol in the same dosage; the urine became sterile in 4 cases, 2 of which had failed previously to respond to either drug given alone. Thus 12 out of 23 cases responded well to chloramphenicol and penicillin, singly or combined. In one of the cases which responded well to penicillin the organism isolated was resistant to the antibiotic *in vitro*; and 4 strains which were sensitive *in vitro* to a combination of penicillin and chloramphenicol were resistant clinically.

It is concluded that penicillin may be combined with chloramphenicol or other antibiotics with benefit in suitable cases; and that the fact that a strain of organism is resistant to an antibiotic *in vitro* does not necessarily rule out the possibility of satisfactory response to the same drug *in vivo*. *F. Hawking*

1089. **Use of Dibenzylethylenediamine Penicillin Administered Orally in Bacterial Infections**

M. H. LEPPER, J. RODRIGUEZ, N. BLATT, and H. W. SPIES. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 175–178, April, 1952. 7 refs.

Results of treatment of infections in 42 patients with dibenzylethylenediamine penicillin are reported. Among 37 patients who had bacterial infections, which generally respond to penicillin therapy, only 2 had a poor response. Satisfactory results can be anticipated with a dose of

250,000 units every 6 hours in young children and 500,000 units every 8 hours in older children and adults.

The only toxic reaction observed was the occurrence of loose stools in 3 patients.—[Authors' summary.]

1090. **Penicillin Sensitivity of Staphylococci**
E. REISS, E. J. PULASKI, W. H. AMSPACHER, and A. A. CONTRERAS. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 611–612, April 17, 1952. 10 refs.

1091. **Antibacterial Action of Oral Aureomycin on the Contents of the Colon of Man**
W. I. METZGER, L. T. WRIGHT, R. F. MORTON, J. C. DILORENZO, and M. MARMELL. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 91–102, Feb., 1952. 21 refs.

To study the value of aureomycin in preparation of the gastro-intestinal tract for surgical treatment the authors gave the drug by mouth in doses of 1 g. three times daily for an average of 3 to 4 days to 15 patients at Harlem Hospital, New York, and the effect on the intestinal flora was carefully evaluated.

The concentration of aureomycin in the stools was found to reach a peak on the last day of treatment, the maximum varying from 4·5 to 21 mg. of aureomycin per g. wet stool. This concentration fell rapidly when the drug was discontinued. The antibiotic was well tolerated, the only side-reactions occurring being nausea and anorexia, followed by vomiting on the third and final day of treatment. In 12 of the 15 cases the coliform organisms, yeasts, and anaerobes (both spore-forming and non-spore-forming) were considerably reduced in number. In 11 cases, however, the reduction of sensitive organisms was followed by a significant increase in the numbers of *Proteus* and of streptococci and staphylococci present in the stool.

The authors conclude that although aureomycin does not sterilize the intestinal contents, it is probably as effective as any single agent available at present for this type of preoperative treatment. *J. W. Czekalowski*

1092. **An Antiviral Substance, Abikoviromycin, Produced by *Streptomyces* Species**
H. UMEZAWAI, T. TAZAKI, and S. FUKUYAMA. *Japanese Medical Journal* [*Jap. med. J.*] **4**, 331–346, Oct., 1951 [received May, 1952]. 6 refs.

In a report from the National Institute of Health, Tokyo, the authors describe their work on antiviral agents, with reference to the problem of evolving a satisfactory technique for the assessment of the activity of such agents, which tend to be specific. In examining *Streptomyces* spp. they obtained material effective against the virus of western equine encephalomyelitis in mice from 13 strains, 12 of which belonged to a new species (*Str. abikoensum*) found in garden soil, the remaining organism being *Str. rubescens*. This material, which has been named abikoviromycin, was tested by being mixed with a 1 in 10^6 dilution of fresh infected mouse brain in broth and injected into mice after standing for 15 minutes. Survival for 7 days was the criterion adopted. It was soluble in ethyl acetate or ether at *p*H 7 and was extracted after 3 days shaking at 27° C. and purified chromatographically. It was weakly antibacterial in concentrations of 62·5 to 1,000 μg. per ml., but was active against western equine encephalomyelitis virus at about 1 in 8×10^6. It was also effective against the virus of eastern equine encephalomyelitis, but not against those of Venezuelan equine and Japanese B encephalomyelitis. The LD50 for mice of 12 to 13 g. was about 0·1 mg. intravenously and 1·25 mg. subcutaneously.
Malcolm Woodbine

1093. **Subtilin and the Spores of *Clostridium botulinum***
O. B. WILLIAMS and T. C. FLEMING. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 75–78, Feb., 1952. 10 refs.

In an investigation carried out at the University of Texas the effect of subtilin on the spores of *Clostridium botulinum* was studied by means of two series of experiments. In the first series the relative sensitivity of spores of different strains was determined by measuring the effect on growth in Ayres's medium of increasing amounts of the antibiotic. It was found that there were differences in susceptibility between the strains, as shown by differences in the amount of subtilin required to restrain germination and growth from small and large inocula.

The second series of experiments was designed to determine whether subtilin was sporistatic or sporicidal. When inocula of 1,000,000 spores were made into Ayres's medium containing 120 p.p.m. of subtilin and into control tubes of medium without subtilin, all the latter, but none of the former, showed growth at the end of 72 hours' anaerobic incubation at 32° C. However, on re-incubation after the removal of subtilin by washing, it was found that the full original inoculum had survived, and the prompt growth obtained indicated the absence of injury to the spores as a result of the exposure to the antibiotic. It is therefore concluded that the action of subtilin is entirely sporistatic. *J. W. Czekalowski*

1094. **Subtilin Considered as a Germicidal Surface-active Agent**
L. E. SACKS. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 79–85, Feb., 1952. 2 figs., 18 refs.

It has been shown by Anderson (*J. invest. Derm.*, 1947, **8**, 25) that subtilin possesses marked surface activity, but whether this is responsible for its antibacterial properties has not yet been determined. In experiments at the Western Regional Research Laboratory of the U.S. Department of Agriculture the author has demonstrated that subtilin brings about a rapid and permanent reduction in the metabolic activity of *Micrococcus pyogenes* var. *aureus* and *M. conglomeratus* and is strongly bactericidal, causing bacteriolysis; no evidence of bacteriostatic activity was obtained. It exhibits all the properties considered as typical of tyrocidine and the germicidal surface-active agents, and it is suggested that it be included in the same group. Subtilin is water-soluble and retains its activity in the presence of lecithin and cephalin preparations. *J. W. Czekalowski*

Infectious Diseases

1095. **Terramycin in the Treatment of Human Brucellosis**
M. Ruiz Castaneda and G. Guerrero Ibarra. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 86–90, Feb., 1952. 9 refs.

In a series of 84 cases of infection with *Brucella melitensis* treated in Mexico with terramycin the results were considered to be satisfactory. Although recurrences were fairly frequent (30 to 50%), they were readily checked by repetition of treatment with either terramycin or aureomycin. The effectiveness of terramycin seemed comparable to that of aureomycin. The authors recommend a prolonged course of treatment, a dose of 5 g. being given daily for periods of 5 days at 5-day intervals, the total dose being 30 to 40 g. It was found, however, that even with doses of 0·75 g. a day the results were satisfactory. *J. W. Czekalowski*

1096. **Chloramphenicol in Treatment of Typhoid in China**
F. G. Scovel. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1188–1193, April 5, 1952. 20 refs.

In this paper the author describes the treatment with chloramphenicol of 74 patients suffering from typhoid fever. In 31 cases the diagnosis was confirmed by blood or bone-marrow culture. The patients were given 1·5 to 3·0 g. of chloramphenicol followed by 0·25 g. 2-hourly until the temperature subsided, when the same dose was given 4-hourly. The average duration of treatment was 3·5 days. Haemorrhage occurred in 7 cases and relapse in 6; there was abortion in 3 out of 4 pregnant women; in 1 patient there may have been bowel perforation. Three deaths occurred. There did not appear to be any difference between the response of those with bacteriaemia and those without. *T. Anderson*

1097. **Leptospiral Meningitis**
P. B. Beeson and D. D. Hankey. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 575–583, April, 1952. 1 fig., 11 refs.

After a short review of the epidemiology and clinical manifestations of leptospirosis and of the laboratory methods used in its diagnosis, the authors discuss the clinical features of leptospiral meningitis as seen in 7 cases observed by them at the Grady Hospital and Lawson Veterans Administration Hospital, Atlanta, Georgia, and in 17 other cases in which serological evidence of leptospiral infection was obtained in their laboratory, but which were not observed personally. The infecting species proved to be *Leptospira canicola* in 12 cases, *L. icterohaemorrhagiae* in 10, and *L. pomona* in 2. The age distribution of these 24 cases indicated that the meningeal form of leptospirosis is a disease of young persons. The patients' ages ranged from 10 to 55 years, but 19 of the 24 were under 30, whereas the ages of 12 patients who suffered from classical Weil's disease during the same period ranged from 25 to 63, with an average of 42 years. The incidence was highest in summer, and 10 of the cases occurred during the month of August.

A similar clinical picture was produced by all 3 species, and comprised fever, chills, headache, muscle pains, and stiffness of the neck. In about half the cases the patient had a cough, accompanied in one instance by haemoptysis. Suffusion of the conjunctivae was present in 4 cases, in 2 of which there were also areas of conjunctival haemorrhage. None of the patients developed jaundice, and the urine was normal and the leucocyte count within normal limits in all cases. The number of cells in the cerebrospinal fluid was always increased after the end of the first week, but seldom exceeded 300 per c.mm. The protein concentration was also raised, but only to a moderate extent. In this series the fever seldom followed the biphasic course which is often a characteristic feature of leptospiral meningitis, but was usually continuous in type. The total duration of fever varied from 5 days to 3 weeks, but was 8 to 12 days in the majority of cases. No relapses occurred, and no late sequelae were observed. *J. C. Broom*

1098. **A Study of the Therapeutic Effects of Some Amebacidal Drugs**
W. A. Sodeman and P. C. Beaver. *American Journal of Medicine* [*Amer. J. Med.*] **12**, 440–446, April, 1952. 4 refs.

A study of the effect of certain amoebicidal drugs was carried out at a large school for the feeble-minded in Mississippi, where a large group of patients could be kept under conditions of strict quarantine. There were 350 individuals of all ages in 5 dormitories. Single stool specimens from the patients and from some attendants were examined, and then the patients and the attendants, totalling 341, were given one or other of the following drugs under close supervision: "diodoquin" (di-iodohydroxyquinoline), 0·63 g. 3 times daily for 20 days; chiniofon, 1·0 g. 3 times a day for 8 days; "milibis", 0·5 g. 3 times daily for 8 days; thioarsenites, 0·1 g. 3 times a day for 10 days. These doses were given to adults. The stools were re-examined 2, 3, and 4 to 5 weeks after treatment was completed.

Detailed tables give the results for all the different amoebae present, but they may be briefly summarized as follows. Chiniofon was given to 117 patients; 10·2% of the stools contained *Entamoeba histolytica* before treatment, and 1·7% (2 patients) afterwards (examination at 2 weeks). Diodoquin was given to 57 patients; 15·8% of the stools showed infection before treatment, and none afterwards. Milibis was given to 138 patients; 34% of the stools showed infection before treatment, and none afterwards. Thioarsenites were given to 29 patients; the stools of 34% showed infection before treatment,

and none afterwards. As regards the non-pathogenic amoebae, none was found after administration of thioarsenites; after milibis had been given *Entamoeba coli* and *Endolimax nana* were much reduced in number and *Iodamoeba bütschlii* was absent; after administration of diodoquin the number of *E. coli* was much reduced, *I. bütschlii* was absent, but *E. nana* was not affected; after chiniofon *E. coli* and *I. bütschlii* were somewhat reduced in number, but *E. nana* was unaffected. One year later, two stools were examined from each of 149 patients who had been treated with diodoquin or milibis; neither *E. histolytica* nor *I. bütschlii* was found.

Untoward reactions to the drugs were relatively uncommon. With chiniofon the usual diarrhoea developed in 11·4% of patients. Diodoquin was discontinued in 2 patients because of severe constipation and a severe generalized eruption respectively, although it is not certain that these complications were due to diodoquin. One patient developed allergic skin reactions to thioarsenites, and 3 had nausea and vomiting during treatment. It is concluded that milibis, thioarsenites, and diodoquin are effective (in that order) against *E. histolytica*, but that chiniofon is less reliable.

[This is a valuable study which contains more detailed information than can be given in an abstract.]

F. Hawking

VIRUS DISEASES

1099. **Management of Respiratory Infections in Patients Severely Paralysed by Poliomyelitis**

F. H. STEVENSON. *Lancet* [*Lancet*] **1**, 845–847, April 26, 1952. 1 fig.

Respiratory infections ordinarily regarded as mild are a grave danger in patients with a severe degree of residual paralysis of the respiratory muscles after poliomyelitis. The bronchi are readily involved and, because of the inability to cough adequately, atelectasis of varying degrees is common. At this stage physiotherapy fails to clear the lumina, and bronchoscopy is necessary. The fear of repeated bronchoscopy makes every cold a terrifying experience for the patient. To overcome the difficulty the following routine has been adopted at the Royal National Orthopaedic Hospital, Stanmore: (1) On admission a radiograph is taken in inspiration and expiration on the same film, in order to have a record of the diaphragmatic excursion. Vital capacity is also determined on admission and again every 6 weeks. (2) The slightest upper-respiratory-tract infection is immediately treated with 500,000 units of penicillin 8-hourly, and cultures of the throat and nose are taken so that alternative chemotherapy can be used if necessary. (3) The physiotherapists have been taught the possible complications of an upper respiratory infection and how to recognize the signs of accumulation of mucus locally and of consolidation and collapse by examination of the chest; and they are also taught the essentials of bronchial anatomy as related to postural treatment. (4) The patients are taught to recognize and report the slightest symptom of respiratory infection. When catarrhal bronchitis has developed it is the duty of the physiotherapist to attend to the patient 4 or more times a day to encourage him to clear excess mucus by cough, and to assist him by holding the chest and pushing in unison with the patient's efforts and by slight tilting of the bed to 20 degrees above the horizontal. The patient will often report blockage of a bronchus, which can usually be cleared by assisted coughing if treated immediately. Bronchoscopy is now seldom necessary.

John Crofton

1100. **"Priscoline" in Acute Poliomyelitis: Clinical Observations of Seventy-one Patients**

A. C. LABOCCETTA and K. E. DAWSON. *Journal of the American Medical Association* [*J. Amer. med Ass.*] **148**, 1083–1085, March 29, 1952. 5 refs.

"Priscoline" (2-benzyl-2-imidazoline hydrochloride) was given to 71 patients suffering from acute poliomyelitis with muscle pain and spasm. The drug was usually administered orally or intramuscularly every 4 hours. The dose was adjusted to the age of the patient: for children aged 1 to 4 years the range was 50 to 80 mg. orally and 25 to 50 mg. by intramuscular injection; for those aged 5 to 15 years it was 50 to 100 mg. orally and 25 to 50 mg. intramuscularly; and for patients over the age of 15 it was 50 to 100 mg. orally and 50 to 75 mg. intramuscularly. Complete relief of pain and complete, or nearly complete, relief of spasm were observed in 19 patients; complete relief of pain without striking relief of spasm was obtained in 26 patients. The drug was without effect in 26. Reactions to the drug were nausea or vomiting in 17, marked flushing of the skin in 21, sweating in 7, chills in 6, diarrhoea in 1, palpitation in 1, and urticaria in 1.

R. S. Illingworth

1101. **Acute Epidemic Haemorrhagic Fever**

D. D. BEARD. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 294–295, March 1, 1952.

In the summer and autumn of 1951 there were some 200 cases of a disease among the United Nations forces in Korea of which the following were the main symptoms: a prodromal stage of 3 days with anorexia, vomiting, and diarrhoea; a rapid rise in temperature to 103° to 105° F. (39·4° to 40·6° C.); continuous high pyrexia for 3 to 5 days, associated with severe headache, sore blood-shot eyes, blurred vision, a petechial rash over the face and the upper part of the trunk, and a marked tendency to bleeding from the gums, nostrils, bowels, and kidneys; a rapid lysis followed by a slow convalescence. Mortality was from 12 to 14%. Case-to-case infection probably did not occur. Detailed clinical features and laboratory findings are given for one case only. [Serological tests to exclude rickettsial and leptospiral infections were presumably done, but are not mentioned.]

The disease is said to resemble one which was reported in 1939 among Japanese troops in North Manchuria, and which was shown by Kitano and others [no reference given] to be due to a virus transmitted by the bite of a mite for which the field mouse is the host. No specific treatment has been found. The provisional name of "acute epidemic haemorrhagic fever" is suggested.

L. J. M. Laurent

1102. **The Effect of Rubella Virus on the Human Embryo.** (Zur Wirkung des Erregers des Rubeolen auf den menschlichen Keimling)
G. TÖNDBURY. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **7**, 105–135, April, 1952. 14 figs., 20 refs.

The author examined 6 embryos of different ages whose mothers had developed rubella between the 35th and 51st days of pregnancy. The rubella virus is capable of passing the placental barrier without damaging the chorionic epithelium, the danger period for the foetus being the first 3 months of pregnancy. The embryos did not show any signs of generalized disease, but there was evidence of disturbance of the development of various organs, such as the lens, the inner ear, and the enamel organ. Although the development of the eyes appeared to be normal, a more or less pronounced degeneration of the lens fibres was found, associated in one case with microphthalmia and in another with cataract. While the histological changes in the lens were present even in an embryo examined within 17 days of the mother developing the disease, the sensory cells of the inner ear and the cells of the enamel organ showed signs of destruction only in one embryo which was not born until 222 days after the appearance of the rubella rash.

Franz Heimann

1103. **Herpes Zoster: its Treatment with Protamide**
F. C. COMBES and O. CANIZARES. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **52**, 706–708, March 15, 1952. 2 refs.

The evaluation of any method of treatment of herpes zoster is difficult, since the condition is self-limiting and the course of the disease and the severity of the accompanying pain cannot be predicted accurately in the early stages. During the last 2 years the authors have treated 50 cases at Bellevue Hospital, New York, with intramuscular injections of " protamide ", a denatured proteolytic enzyme obtained from the mucosal layer of hog stomach, the use of which was suggested by its effectiveness in relieving the lightning pains of tabes dorsalis. From 1 to 16 injections (1·3 ml.) were given at intervals varying from 6 to 48 hours. The results were excellent or satisfactory in 39 cases, particularly in respect of relief of pain, which was almost immediate. In most cases this improvement lasted for several days, but in others it lasted only for a few hours immediately following the injection. None of the patients who responded satisfactorily developed post-herpetic neuralgia. There were no untoward side-effects. *H. R. Vickers*

1104. **Herpes Simplex Virus as the Cause of Fulminating Visceral Disease and Hepatitis in Infancy**
W. W. ZUELZER and C. S. STULBERG. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **83**, 421–439, April, 1952. 6 figs., 15 refs.

The authors report 8 fatal cases of systemic infection by the virus of herpes simplex, 5 in newborn and 3 in older infants, all but one of which were seen at the Children's Hospital of Michigan. There was an initial infection by the virus of the eyes in 3 cases, the mouth in 3 cases, and the skin possibly in one case, but no local lesion was demonstrable in the remaining case. This was followed by jaundice, a marked bleeding tendency, and respiratory distress with the coughing up of large quantities of yellow, and later bloody, mucus. The liver was usually enlarged, the spleen sometimes. Death supervened within a few days and was directly attributable to the disease in all but 2 cases, both in older infants who died from unrelated causes.

Histological appearances characteristic of herpes infection were demonstrated post mortem in all 8 cases in the local lesion (when present) and also in distant organs, where the findings were suggestive of a blood-borne infection. Massive areas of necrosis and haemorrhage were found in the lungs, stomach, liver, spleen, lymph nodes, bone marrow, adrenal glands, kidneys, and brain. In certain cases, particularly those in older infants, some of these organs were unaffected, but the liver was involved in every case and the spleen in all but one. In every affected organ typical intranuclear inclusion bodies were demonstrated. A photograph of the gross appearance of the liver in one case is reproduced.

Isolation of the virus of herpes simplex from the liver of one patient was convincingly demonstrated by inoculation into the cornea of the rabbit, by growth on the chorio-allantoic membrane of chicks, and by neutralization of the later growth by specific antiserum. The authors suggest, therefore, that this virus may cause a fatal blood-borne infection secondary to, or in the absence of, the more common localized infection, and that this may give rise to visceral lesions which are more widespread in the newborn than in later infancy, when they may be confined to the liver. *H. G. Farquhar*

1105. **Aureomycin, Chloromycetin and Terramycin in Treatment of Acute Viral Hepatitis**
J. W. COLBERT, L. BUNGARDS, and M. KNOWLTON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **79**, 339–343, March, 1952. 2 refs.

The results of the treatment of hepatitis in young males here described were obtained at the 98th General Hospital, U.S. Army of Occupation in Germany. All the cases were classified as viral hepatitis, although many were probably undifferentiated homologous serum hepatitis. Of the 58 patients, 24 received 1 g. aureomycin orally; 4 received the same dose orally and 100 mg. intravenously; 10 received 50 mg. chloramphenicol per kg. body weight initially and then 500 mg.; 20 received 1·25 g. terramycin orally; there were 54 controls who were given placebos. All the doses were given at 6-hourly intervals for 10 days. The patients were examined daily and weighed weekly. The serum bilirubin and γ-globulin levels were estimated and the cephalin–cholesterol flocculation and thymol turbidity tests performed on admission and twice weekly thereafter. The bromsulphalein retention test was carried out weekly until 2 determinations of 6% or less were obtained. Patients were maintained on a diet of 4,200 Calories which contained 190 g. protein, 607 g. carbohydrate, and 114 g. fat, and included supplementary vitamins and brewer's yeast.

Statistical analysis of the results shows that the course of acute viral hepatitis in young adult males was unchanged by aureomycin and chloramphenicol. Although terramycin was associated with a more rapid recovery of liver function, it is doubtful whether this result was significant. *Malcolm Woodbine*

1106. **Studies on the Agent of Infectious Hepatitis. III. The Effect of Skin Tests for Infectious Hepatitis on the Incidence of the Disease in a Closed Institution**
M. E. DRAKE, C. WARD, J. STOKES, W. HENLE, G. C. MEDAIRY, F. MANGOLD, and G. HENLE. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 231–239, March 1, 1952. 11 refs.

An investigation was carried out in a mixed residential school in Maryland at the onset of an epidemic of infective hepatitis with the object of studying the meaning of positive and negative reactions to skin tests in terms of immunity to the disease. Amniotic fluid from chick embryos infected with the virus of infective hepatitis was used, after irradiation with ultraviolet light, as the antigen, and about a quarter of the 1,300 children in the school were tested.

The original object was not attained, but it was noticed that jaundice subsequently occurred in only 1·6% of the children tested as against 13·6% of the other children. Taking into account the method of selecting the children for testing, the authors conclude that the injection of antigen must have reduced their susceptibility to infective hepatitis, there being two main possibilities: (1) that partial immunity was produced by the inactivated virus and reinforced by natural infection, the resulting infection not being severe enough to produce jaundice; and (2) that the virus in the skin-test antigen was only partially inactivated. *Peter Story*

See also Tuberculosis, Abstract 1131.

INFECTIOUS DISEASES OF UNKNOWN AETIOLOGY

1107. **Corticotrophin and Cortisone in the Treatment of Sarcoidosis.** (ACTH und Cortison bei Sarcoidosis)
B. CARTENSEN and L. NORVITT. *Acta Societatis medicorum Upsaliensis* [*Acta Soc. Med. upsalien.*] **56**, 197–208, 1952. 2 figs., 1 ref.

Four cases of sarcoidosis are described, the first in a woman of 53 who was admitted to a sanatorium with fever and enlarged hilar lymph nodes. She developed neurological symptoms with bilateral facial palsy; the cerebrospinal fluid showed a pleocytosis and a protein content of 110 mg. per 100 ml. There was no positive evidence of tuberculosis and the case was considered to be one of sarcoidosis. She was given 850 mg. of corticotrophin in 1 month; the nervous signs disappeared and the general symptoms died down, but the hilar nodes were unaffected; later a course of 2,200 mg. of cortisone had no effect on them. The second patient, a woman of 33, first had enlarged lymph nodes in the neck, and radiography showed enlarged hilar lymph nodes and increased lung markings; a diagnosis of tuberculosis was made. But 8 months later, when she was much worse with widespread enlargement of the lymph nodes, a node was removed for biopsy and showed typical sarcoidosis. When treated with alternate courses of corticotrophin and cortisone she showed great improvement in the general condition, and the peripheral lymph nodes were no longer enlarged. The changes in the hilar nodes and the lungs persisted, and were still present 4 months after cessation of treatment.

The third patient, a man of 47, had an affection of the joints, and later developed fever; radiography showed increased hilar lymph-node shadows and parenchymatous lung changes. Tests for tubercle bacilli were negative, and treatment with calciferol was ineffective. He was given corticotrophin with good results so far as the joint affection and the remission of fever were concerned, but there were no significant changes in the *x*-ray picture of the lungs. This case was diagnosed as sarcoidosis, although this could not be confirmed by biopsy. The fourth patient was a man with skin lesions, intermittent fever, and massive albuminuria; radiography of the chest showed enlarged hilar lymph nodes and a miliary type of lung infiltration. Biopsy of a skin lesion showed sarcoidosis. He was treated with 390 mg. of corticotrophin in 12 days followed by 2,450 mg. of cortisone in the next month. The skin lesions and the albuminuria disappeared and the miliary lung infiltration also resolved; but, as in the other cases, the hilar nodes remained enlarged. *M. C. G. Israëls*

1108. **"Periodic Fever": a Report of 14 Cases, 8 with Renal Complications.** (La maladie périodique. (Sur 14 cas personnels dont 8 compliqués de néphropathies))
H. MAMOU and R. CATTAN. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 1062–1070, April 2, 1952. 13 refs.

The authors describe 14 cases of "periodic disease" which they have seen during the last 20 years. The disease may take the form of periodic attacks of acute arthritis, abdominal pain, or malaria-like fever with the crises occurring about every 7 days. The disease appears to occur in families, and although it may continue for many years without affecting the health of the patient, signs of chronic renal disease may appear. Other workers have tried to link the disease with recurrent thrombocytopenia, or granulopenia and periodic paralysis, but the authors' cases do not fit into any of these groups. The clinical details of the 14 cases are given; 10 of these occurred in one family, and 6 patients died from renal complications; 16 other cases collected from the literature are reviewed. In a discussion of the nature of the disease the possibility of an allergic or hormonal factor is considered. Other workers have found some relationship between the crises and oestrogen and 17-ketosteroid excretion, but the authors doubt the significance of this as it does not explain the occurrence of the disease in families and infants. Finally, in discussing the importance of the renal complications, they consider the possibility of amyloidosis, but come to no definite conclusion. The differential diagnosis is fully discussed. *R. F. Jennison*

Tuberculosis

1109. **Tuberculous Pericarditis**
T. M. MYERS and M. HAMBURGER. *American Journal of Medicine* [*Amer. J. Med.*] **12**, 302–310, March, 1952. 13 refs.

The course of so-called primary tuberculous pericarditis in 3 cases treated at the Cincinnati General Hospital with streptomycin is described and compared with that in 9 cases in which chemotherapy was not employed. Of the former all recovered completely, whereas of the latter group, 4 recovered spontaneously and 5 died of miliary dissemination or of heart failure within a few months. On the basis of these cases the general conclusion is reached that while the outcome in tuberculous pericarditis is in any case uncertain, treatment with streptomycin (1·0 g. daily for 2 or 3 months) makes healing and drying very much more likely and delays relapse.
G. F. Walker

1110. **Tuberculous Peritonitis. A Follow-up Study of 169 Cases**
T. KAHRS. *Journal of the Oslo City Hospitals* [*J. Oslo City Hosp.*] **2**, 65–71, April, 1952. 12 refs.

The author presents a follow-up study of 169 cases of tuberculous peritonitis treated in the Ullevål Hospital, Oslo, between the years 1930 and 1948. The disease was relatively acute in onset and was most often seen in the age group 20–30 years, being more common in women (58%) than in men (42%). Three types of the disease are recognized: (1) serous, (2) fibrotic, and (3) purulent, although it may appear in mixed forms. The purulent type was rare in this series, being found in only 9 patients. The symptoms of tuberculous peritonitis vary according to the type of lesion present, but pain and fever occurred in about two-thirds of these cases. Diagnosis is difficult, and of this series only in 13% was the correct diagnosis made on admission to hospital, many of the cases being confused with other acute abdominal conditions. There were 45 cases of tuberculous polyserositis, 28 of which were in men and 17 in women. In 60 cases (33 in men, 27 in women) there was an intestinal focus. Of the 99 women in this series, 51 most probably developed peritonitis from a tuberculous salpingitis. Mesenteric lymph nodes were the probable focus in 8 cases. In 62 cases out of the 94 in which particulars were available, peritonitis developed within 5 years of the primary infection. The over-all prognosis is not good: 64 patients died within a year after admission to hospital and 13 died of tuberculous disease during subsequent years; 90 patients were alive at the end of an observation period varying from 2½ to 20½ years. Complete cure is reported in 28 males and 32 females. Prognosis in the purulent type of the disease is very bad. The chance of pregnancy after tuberculous peritonitis is small, especially in those women whose disease is preceded by tuberculous salpingitis.
T. Marmion

DIAGNOSIS

1111. **Evaluation of Hemolytic Modification of Middlebrook–Dubos Test for Tuberculous Antibodies**
B. GERSTL, D. KIRSH, E. M. ANDROS, J. W. WINTER, and L. E. KIDDER. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **22**, 337–344, April, 1952. 15 refs.

Certain aspects of the Middlebrook–Dubos haemagglutination test for tuberculosis antibodies which detract from its clinical value were investigated at the Veterans Administration Hospital Laboratory, Oakland, California. The finding of earlier workers that an injection of tuberculin can stimulate the production of antibodies in a considerable proportion of non-tuberculous individuals was confirmed. The authors also confirmed that a substantial proportion of patients with active tuberculosis yield negative tests, even when the more sensitive haemolytic modification of the reaction is employed. Attempts to render the test more sensitive by procedures designed to enhance the agglutination reaction, entailing either pre-treatment of the erythrocytes with Forssman antibody or the use of polyvinyl pyrrolidone, were unsuccessful. The possibility that the negative or low titres observed in the sera of tuberculous individuals were due to blocking antibodies was also excluded.
J. E. M. Whitehead

See also Bacteriology, Abstracts 1076–7.

1112. **Agglutination of Sensitized Sheep Erythrocytes and Collodion Particles by Tuberculous and Normal Sera**
C. A. COLWELL and G. PITNER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 238–244, Feb., 1952. 1 fig., 23 refs.

In this study reported from the Veterans Administration Hospital, Hines, Illinois, old tuberculin (4 times standard strength) and an aqueous extract of acetone-treated tubercle bacilli were used to sensitize sheep erythrocytes, and the latter extract also used to sensitize collodion particles, which were then used for the Middlebrook–Dubos reaction in tuberculosis. Contrary to the findings of other workers, repeated intradermal tuberculin tests in tuberculin-negative individuals failed to affect the titre of their serum. Although higher titres were found significantly more frequently in sera from tuberculous patients than in sera from non-tuberculous persons, the authors conclude that these tests were not sufficiently specific to be useful in the diagnosis of tuberculosis.
J. E. M. Whitehead

1113. **Serological Reactions in Tuberculosis: with Particular Reference to the Haemagglutination Test**
R. J. CUTHBERT. *Glasgow Medical Journal* [*Glasg. med. J.*] **33**, 107–114, April, 1952. 1 fig., 18 refs.

The literature on the haemagglutination test in tuberculosis has been reviewed. The results of a study of the test in persons suffering from tuberculous and non-

tuberculous diseases are reported. Of cases with active tuberculosis significant agglutination titres (1:8 or over) were obtained in only 62%; in a further 11% agglutination occurred at lower titres, while in 27% agglutinins were absent. Among the non-tuberculous controls "false-positive" reactions (at a titre of 1:8 or more) were present in 17% and low-titre agglutination occurred in a further 47%.

Possible explanations are given for the occurrence of negative reactions in cases of active tuberculosis and of "false-positive" reactions in non-tuberculous individuals.

It is suggested that the haemagglutination test in its present form has little practical usefulness.—[Author's summary.]

PULMONARY TUBERCULOSIS

1114. **Preliminary Observation on the Value of *iso*-Nicotinic Acid Hydrazide in the Treatment of Tuberculosis.** (Primi rilievi sul valore terapeutico dell'idrazide dell'acido isonicotinico nella tubercolosi)
V. MONALDI. *Archivio di Tisiologia* [*Arch. Tisiol.*] **7**, 183–192, March, 1952. 2 figs.

The conclusions of other workers on the antituberculous activity of *iso*nicotinic acid hydrazide *in vitro* and in experimental animals are confirmed by the author [but he makes no reference to the published work]. Between March 1 and April 7, 1951, 350 patients with tuberculosis, mainly pulmonary, were treated with the drug, the usual dose being 200 mg. daily. On the strength of 5 weeks' experience, the author feels entitled to conclude that the results with *iso*nicotinic acid hydrazide, though impressive, are not so good as those obtained with streptomycin. *M. Daniels*

1115. **Tuberculosis Chemotherapy with Hydrazine Derivatives of *iso*Nicotinic Acid**
I. J. SELIKOFF and E. H. ROBITZEK. *Diseases of the Chest* [*Dis. Chest*] **21**, 385–438, April, 1952. 7 figs., 12 refs.

At the Sea View Hospital, Staten Island, New York, 92 tuberculous patients were treated with *iso*nicotinic acid hydrazide or its *iso*propyl derivative for from 4 to 15 weeks. The prognosis in every case was considered poor, and the criterion for inclusion in the group was that a case was unlikely to respond to any possible standard programme of treatment. The sputum of all patients was positive for tubercle bacilli, and 44 of them were febrile.

Dosage was from 2 to 4 mg. per kg. body weight for *iso*nicotinic acid hydrazide and from 2 to 10 mg. per kg. for its *iso*propyl derivative. All the patients benefited from the drug, and in every case fever and toxicity were rapidly eliminated. There was a great improvement in the general sense of well-being, and appetite increased so markedly that it is now estimated that the dietary intake of these patients is 5,000 Calories, with 180 g. of protein. There was an average weight gain of 18 lb. (8·2 kg.) in an average of 9 weeks. The greater weight gains occurred in the group receiving the higher doses. Cough in all cases, except for one patient who had a broncho-pleural fistula, was markedly alleviated by the end of the 2nd week, and sputum was greatly diminished and became less purulent. In 25% of the patients the sputum became negative (concentrated smear), but results of sputum cultures are not yet known. In a further 28% of patients only an occasional positive sputum was found. Radiological examination showed that among the 92 cases cavity closure occurred in 2, but there was reduction in cavity size in 33 cases and clearing of exudative disease in 17. Extension of exudation occurred in 4 cases, and one case showed possible cavitation in a previous exudative area.

Among the cases of extrapulmonary lesions 10 patients with tuberculous laryngitis were markedly improved. Good results were also noted in tuberculous otitis media, enteritis, glossitis, and in bone and joint disease. Toxic effects were minimal, but leg twitching, increased reflexes, vertigo associated with a fall in systolic pressure, constipation, and reflex disturbances of micturition were noted. *G. M. Little*

1116. **The Prevention of Streptomycin Resistance by Combined Chemotherapy**
MEDICAL RESEARCH COUNCIL. *British Medical Journal* [*Brit. med. J.*] **1**, 1157–1162, May 31, 1952. 1 fig., 3 refs.

In a previous Medical Research Council investigation (*Brit. med. J.*, 1950, **2**, 1073; *Abstracts of World Medicine*, 1951, **9**, 442) it was shown that the resistance of *Mycobacterium tuberculosis* to streptomycin is less likely to develop when 20 g. of PAS (as the sodium salt) is given daily, but that this high dosage causes gastro-intestinal symptoms in about half the patients treated. The present investigation was undertaken to determine whether smaller doses of PAS would be as effective in preventing the development of resistance, and was carried out by the clinicians and pathologists of 10 hospitals in England and Wales under the coordination of the M.R.C. Tuberculosis Research Unit, the radiological results being assessed by the same radiologist in all cases, and the findings being subjected as a whole to statistical analysis. Altogether 115 patients aged between 15 and 30 were investigated, all of whom had acute, progressive, bilateral, pulmonary tuberculosis which was believed to be recent in origin and unsuitable for collapse therapy. The diagnosis was proved bacteriologically.

The patients were divided at random into three groups, and were all treated under similar conditions except that 42 patients (Group SP 20) received a daily dose of 20 g. of sodium PAS, 39 (Group SP 10) received 10 g., and 34 (Group SP 5) received 5 g. The PAS was given by mouth 4-hourly from 8 a.m., and in all three groups streptomycin, 1 g., was given daily by intramuscular injection at 8 a.m. This combined therapy was started after an initial week of observation and was continued alone for 3 months; during the second 3 months of the trial additional treatment was carried out where necessary, any further chemotherapy being given in the same dosage as in the first 3 months. There was no significant difference between the groups in respect of changes in temperature, general condition, erythrocyte

sedimentation rate, or radiological appearances at the end of either 3-month period. Tests were carried out at monthly intervals for the presence of streptomycin-resistant strains of *M. tuberculosis*. In the third month such strains were found in only 4% of cases in Group SP 20, compared with 8% in Group SP 10 and 32% in Group SP 5; in the sixth month the corresponding figures were 7%, 30%, and 36% respectively. When only strongly resistant strains were considered, the differences were even more marked. Gastro-intestinal disturbances were more frequent with the highest dosage of PAS (52% of cases in Group SP 20 compared with 12% in Group SP 5), but it is recommended that a dose of 20 g. of PAS daily should be given in every case in which it is tolerated, as it is undoubtedly the most effective for preventing the development of streptomycin resistance.

T. Marmion

1117. **Chemotherapy of Pulmonary Tuberculosis in Young Adults. An Analysis of the Combined Results of Three Medical Research Council Trials**
M. DANIELS and A. B. HILL. *British Medical Journal* [*Brit. med. J.*] **1**, 1162–1168, May 31, 1952. 4 figs., 7 refs.

The findings in 3 trials organized by the Medical Research Council's Streptomycin in Tuberculosis Trials Committee between 1947 and 1951 are analysed. The purpose of Trial A was to assess the value of streptomycin in the treatment of pulmonary tuberculosis compared with that of bed rest, 55 patients being given 2 g. of streptomycin daily, the control group consisting of 52 cases. In Trial B the effect of PAS, alone and in combination with streptomycin, was compared with that of streptomycin alone (54 cases given 1 g. of streptomycin daily, 59 given 20 g. of PAS daily, and 53 given 20 g. PAS and 1 g. streptomycin daily). Trial C (*see* Abstract 1116) showed that 20 g. PAS daily was the most effective dose for preventing the development of resistance to streptomycin in the infecting organism. All trials were carried out under similar conditions and all patients had a similar type of disease.

In all the groups given chemotherapy the radiological results were better than in the group treated with bed rest alone, the best results being obtained when PAS was given with streptomycin; the dosage of PAS (5 g., 10 g., or 20 g. daily) made no appreciable difference to the degree of radiological improvement obtained. Groups given streptomycin alone fared better than those given PAS alone, but streptomycin resistance developed more frequently in those patients receiving streptomycin alone: thus in the fourth month of treatment with 2 g. of streptomycin daily highly resistant organisms had developed in 78% of cases, where 1 g. of streptomycin was given the figure was 45%, while with combined therapy (1 g. of streptomycin and 20 g. of PAS daily) it was only 4%. Moreover, reversion of the organism to drug sensitivity occurred much more often with combined therapy than with streptomycin alone. It was confirmed that prognosis is unfavourable if highly resistant strains develop. Moderate drug resistance seems to be of less clinical significance.

T. Marmion

1118. **The Recovery of Streptomycin-sensitive Tubercle Bacilli from a Patient with Pulmonary Tuberculosis who Had Previously Yielded Highly Resistant Bacilli**
R. S. MITCHELL, E. WOLINSKY, and W. STEENKEN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **36**, 1309–1317, May, 1952. 4 figs., 9 refs.

1119. **Dihydrostreptomycin Sulfate in Pulmonary Tuberculosis. Report on Neurotoxicity**
S. T. ALLISON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **65**, 612–616, May, 1952. 8 refs.

Twenty patients in the age group 45 and over were treated for 4 months with dihydrostreptomycin sulfate in a daily dosage of 1 g. Four to 12 months after completion of treatment it can be stated that no symptoms of vestibular damage were noted at any time and there have been no audiometric changes of significance within the hearing range. There has been no clinical deafness.

In the dosage given and for the time period of the study (4 months), dihydrostreptomycin sulfate appears relatively non-toxic. It seems to be better tolerated by patients over 45 years of age than is streptomycin, in that no dizziness and ataxia have been observed when it has been used in 1 g. daily dosage for no more than 4 months. In the absence of definite information at this time it is probably wiser not to use the dihydrostreptomycin sulfate for a period exceeding 4 months. If, however, the daily dosage is reduced to 1 g. twice a week, it may conceivably be given with safety for 6 or 8 months.—[Author's summary.]

1120. **The Differential Diagnoses in Children of the Pulmonary Manifestations of Primary Tuberculosis and its Immediate Sequelae**
L. G. BLAIR. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **46**, 83–86, April, 1952. 8 figs.

A primary focus of pulmonary tuberculosis is often situated close to a pleural surface and as a result a pleural effusion may appear. The hilar lymph node, owing to ulceration into, or compression of, a bronchus, may cause a segmental atelectasis, the segment involved not necessarily being the one in which the primary focus lies. As healing occurs and the segment becomes aerated, the original focus is again visible, is frequently much smaller, and often shows calcification. Calcification may appear in the hilar lymph nodes. If the collapse persists, bronchiectasis may supervene, which can be recognized by the presence of nearly parallel linear shadows radiating out into the segment which was involved. If a round shadow persists in the lung and there is no lymph-node enlargement the possibility of a primary neoplasm, either benign or malignant, solitary secondary deposits, hydatid cysts, and the extremely rare congenital fluid-containing cysts must be considered. If all the mediastinal lymph nodes are involved—an unusual occurrence in pulmonary tuberculosis in Britain—the possibility of Hodgkin's disease, lymphosarcoma, leukaemia, and Boeck's sarcoidosis must be considered first.

At the stage of the segmental lesion, and in the absence of recognizable lymph-node enlargement, the difficulties

of diagnosis are increased. The lesion can be recognized by the crowding of the vascular markings in the particular segment involved. The commonest cause of a segmental lesion undoubtedly is an ordinary infective process, and in such cases, in contrast to the primary lesion of tuberculosis, rapid and complete resolution will occur. Other causes of segmental collapse include asthma, the temporary blocking of a bronchus by secretion or inhaled foreign body, and ball-valve obstruction, usually due to primary tuberculous infection involving the mediastinal lymph nodes or sometimes to a foreign body. Diagnosis can best be arrived at by means of an expiratory film, or on screening, when it will be noted that the affected portion remains relatively more translucent.

Cavitation may occur in primary tuberculosis and must be differentiated from acute lung abscess. Sputum examination or gastric lavage is the most helpful procedure. In cavitation due to acute infection, softening starts in the centre of an opacity and there is often a fluid level: the surrounding consolidation then disappears and the final appearances are those of a thin-walled cyst, which should be differentiated from a tuberculous cavity. Fibrocystic disease of the pancreas gives rise to a disseminate lesion associated with general emphysema, which is to be differentiated from the acute miliary tuberculosis with opacities of pin-head size: there is practically nothing else in children which gives rise to a similar appearance. Two other unusual forms of disseminate lesion are mentioned—xanthomatosis and primary haemosiderosis.

K. Marsh

1121. **Plombage with Acrylic Resin Balls in Collapse Therapy. (A Study of the Results in 122 Cases.)** (Les plombages aux balles de résine acrylique en collapsothérapie chirurgicale. (Étude des résultats obtenus chez 122 opérés))

H. JOLY and J. VILLEMIN. *Revue de la Tuberculose* [*Rev. Tuberc., Paris*] **16**, 169–179, 1952. 10 figs., 9 refs.

From their experience in a series of 122 cases of pulmonary tuberculosis the authors conclude that plombage with " lucite " balls in conjunction with thoracoplasty or extraperiosteal apicolysis (the " birdcage " operation of Lucas and Cleland) results in effective apical collapse combined with good respiratory function of the lower lobe in a high proportion of cases. In 58 cases in which the balls were used as a temporary plomb between the stages of thoracoplasty there were 2 deaths and 9 unsatisfactory results characterized by lung re-expansion or persistent cavitation. The plomb was left *in situ* after the last stage of thoracoplasty had been completed in 24 severe cases unsuitable for lung resection for various reasons, among which there were 2 deaths and 7 cases of residual cavitation. In 15 cases the plomb was left in permanently after a one-stage, 3-rib thoracoplasty, with good results in 14. The " birdcage " operation with permanent plombage gave good results in 16 cases out of 20, with persistent cavitation in 3 others and failure owing to wound disruption in the remaining one. Remobilization and insertion of a plomb was successful in closing the cavities in 3 out of 4 cases of failed thoracoplasty. The complications included meningitis in one case, pyogenic infection in 4, severe intercostal haemorrhage in 1, and migration of the balls in 3 cases. Late removal of the plomb was effected 9 times, in most cases by choice and not of necessity. *S. F. Stephenson*

1122. **" Reflex " Abdominal Syndromes of Thoracic Origin in Pulmonary Tuberculosis.** (Les syndromes abdominaux " réflexes " d'origine thoracique chez les tuberculeux pulmonaires)

M. BARIÉTY, G. ROSSIGNOL, F. MAGNIN, and L. F. PERRIN. *Revue de la Tuberculose* [*Rev. Tuberc., Paris*] **16**, 1–18, 1952. 24 refs.

The authors have classified abdominal symptoms associated with tuberculous lesions of the chest under the following headings: (1) symptoms and signs resembling paralytic ileus; (2) pain in the right iliac fossa or hypochondrium with associated symptoms, suggestive of appendicitis or cholecystitis; (3) symptoms resembling acute dilatation of the stomach. This classification is accompanied by illustrative case histories. Abdominal symptoms of this kind have been observed in association with pulmonary embolism, major or minor thoracic operative procedures, and a sudden increase of fluid in a pneumothorax. They discuss the differential diagnosis and causation of the symptoms, and suggest treatment.

T. M. Pollock

URINARY TUBERCULOSIS

1123. **Streptomycin and PAS Treatment of Genito-urinary Tuberculosis**

J. K. LATTIMER, A. HERTZBERG, J. HARPER, M. BERMAN, D. BRADLEY, and R. VEENEMA. *Journal of Urology* [*J. Urol.*] **67**, 750–761, May, 1952. 7 figs.

The authors review the results of treatment with streptomycin of 228 cases of urinary tuberculosis seen at the Veterans Administration Hospital, New York. In one group of cases a 4-month course of 2 g. daily was effective initially in rendering the urine negative in nearly 70% of cases, but after a follow-up period of 2 years the condition was found to have relapsed in many of the patients. In other groups receiving smaller doses for a similar period the percentage of cases in which the urine was negative was less, but when PAS was given as well the immediate results improved. With a sustained high dosage vestibular damage was universal, but although tubercle bacilli were not permanently eradicated from the urine, the 4-year survival rate was high.

Since the results indicated that prolonged treatment was desirable in order to secure a permanently sterile urine, the authors instituted a plan whereby patients receive 3 g. of PAS 4 times a day, supplemented with streptomycin, 1 g. every third day, for at least a year; if pyuria persists, treatment is continued for a second or third year. It is considered that this regimen delays the development of streptomycin resistance and controls symptoms; at the same time it is relatively non-toxic, and may check the progress of the disease and permit time for healing. *J. D. Fergusson*

BONE AND JOINT TUBERCULOSIS

1124. **Streptomycin in Bone and Joint Tuberculosis**
D. M. Bosworth and H. A. Wright. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34A**, 255–266, April, 1952. 2 figs., 1 ref.

During the 5-year period in which streptomycin has been used by the authors at the Sea View Hospital, Staten Island, New York, the average number of deaths among patients with bone and joint tuberculosis has been just under 6 a year, compared with an average of 21 a year before the introduction of the drug. Of the total of 26 patients who have died during this period, 5 had not received streptomycin and 5 died from severe disease within 6 weeks of admission, before the full bacteriostatic effect of the drug could be obtained. Treatment with streptomycin (without PAS) was normally continued until recovery occurred, and patients often received several hundred grammes of the drug over a period sometimes measured in years. Deafness occurred in 1·1%, vertigo in 26%, and headache in 2·3%. The last two complications disappeared when the drug was discontinued.

The administration of streptomycin in this series did not obviate the need for surgery: all but 2 of the patients with closed bone or joint lesions eventually required some operative treatment, usually fusion of a joint. Lesions complicated by abscesses were in most cases treated by incision and left to drain. Under this regimen all sinuses so formed eventually healed after periods lasting up to 112 days. Of 96 patients with bone or joint lesions and sinus formation treated with streptomycin, 86 have been followed up, of whom 9 still have a sinus or have had intermittent discharge.

In general the authors conclude that the prognosis of bone and joint tuberculosis has improved greatly since the advent of streptomycin, and although surgical intervention is no less frequently necessary, it is now safer and more efficient. *Peter Ring*

1125. **Tuberculosis of the Bones and Joints, with Special Reference to the Influence of Streptomycin and the Application of Radical Surgical Techniques to Certain Effects and Complications of the Tuberculous Lesion**
E. T. Evans. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34A**, 267–278, April, 1952. 11 figs., 2 refs.

In this paper the author challenges the truth of the following well-established dicta: (1) that the surgical attack on bone and joint tuberculosis must await stabilization of the infection as shown by a favourable response to rest; (2) that where the disease is disseminated, surgery is contraindicated until it appears quiescent; (3) that the presence of an abscess is a contraindication to arthrodesis or bone-grafting; and (4) that the development of serious abscesses or sinuses represents a complication which is often insurmountable.

He supports his thesis with a number of radiographs and case reports, and states that while there is no substitute for long periods of rest, the advent of streptomycin often allows stabilization of the joint at an early date. There appears to be some evidence that the value of streptomycin is increased if given in smaller doses over longer periods of time. Disease confined to the synovial membrane often shows rapid regression after treatment with streptomycin alone. *Peter Ring*

1126. **Streptomycin in the Treatment of Bone and Joint Tuberculosis**
R. I. Harris, H. S. Coulthard, and F. P. Dewar. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34A**, 279–287, April, 1952. 1 fig.

Streptomycin has been used at the Toronto Hospital for Tuberculosis in the treatment of 118 cases of bone and joint infection. The total dosage has varied from 60 to 90 g., although a few cases have received up to 180 g. In several cases vestibular and auditory disturbances necessitated a change to dihydrostreptomycin, but in only 2 had the course to be curtailed. In 42 patients the drug was combined with a surgical procedure—either simple excision of tuberculous tissue or bone grafting. In only 3 cases was healing delayed, and there was no case of persistent sinus. Of 14 patients with uncontaminated sinuses only 2 required excision of the sinus. Secondarily infected sinuses were treated with the appropriate antibiotic or sulphonamide in addition to streptomycin in 18 cases, and only 3 remained unhealed. Treatment of closed lesions with streptomycin alone in 34 cases gave equivocal results: 20 patients showed a definite improvement, but in several others new lesions appeared. Out of 10 patients with bone lesions complicated by miliary spread, in 5 with demonstrable miliary lesions in the lung only the result was good, but only one of the 5 with tuberculous meningitis survived. Sensitivity tests, when cultures were available, showed that resistance was commonly acquired during treatment with streptomycin alone, but in spite of this progress was maintained. *Peter Ring*

1127. **Evaluation of Streptomycin Therapy in a Controlled Series of Ninety Cases of Skeletal Tuberculosis**
E. L. Compere, S. Kleinberg, B. Kleiger, P. H. Moore, M. J. Stewart, and P. B. Wright. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34A**, 288–298 and 329–330, April, 1952. 3 figs., 11 refs.

An analysis is presented of the results of a cooperative investigation carried out on behalf of the U.S. Public Health Service, in which 50 cases of skeletal tuberculosis were treated with streptomycin and their progress compared with that of 40 carefully selected control cases in which streptomycin was not used. The clinical course of the disease was assessed by an independent panel after 15 months, the patients in each group receiving other forms of treatment, including surgery, when appropriate. Judged from radiological evidence alone there was no significant difference in the progress of the two groups, but there was clinical evidence of improvement (mainly in the form of closure of sinuses and increase in the haemoglobin level) sooner and in a larger proportion of cases in the group treated with streptomycin than in the control group. Drainage from sinuses was present after 18 months in 21% of the control

group and 4% of the streptomycin group. As regards functional ability, the result in 17% of each group was classified as excellent, in 54% of those given streptomycin and 36% of the control group as good, and in the rest as bad. One patient from each group died during treatment. *Peter Ring*

1128. **The Treatment of Tuberculous Bone Disease by Surgical Drainage Combined with Streptomycin**
M. S. DEROY and H. FISHER. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34A**, 299–329, April, 1952. 16 figs., 11 refs.

Between 1946 and 1950, 52 patients with closed tuberculous bone lesions were treated by the authors with streptomycin, adequate open drainage with removal of sequestra, and packing of the subsequent sinus. Streptomycin treatment was normally continued for a period half as long [? again] as the period required for the sinus to close. The cases are described in some detail. The results in 37 were excellent, with cessation of bone destruction, closure of all sinuses, and retention of 75% or more of joint movement (or solid fusion when arthrodesis had been performed). With the exception of 2 patients who died, the other results were classified as good. The sinus resulting from operation closed after a period of 3 to 16 weeks. Bone regeneration in children appeared common, and a normal epiphysial plate was often found. The authors stress the fact that a bone lesion commonly progresses despite streptomycin treatment until drainage is instituted.
Peter Ring

TUBERCULOUS MENINGITIS

1129. **Chronic Forms of Tuberculous Meningitis.** (Хронические формы туберкулезного менингита)
D. C. FUTER. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **52**, 46–53, No. 2, 1952. 7 figs.

Various forms of chronic tuberculous meningitis may be described in relation to streptomycin therapy which, it is claimed, is effective in 60 to 70% of cases. As a result of the longer survival of patients under treatment with streptomycin the pathological process can now be observed over a considerable period, and conclusions drawn as to the reaction of the meninges to the infection. The account here given is based on the necropsy findings in 69 cases of tuberculous meningitis in patients who had been under observation and treatment for periods ranging from 112 days to nearly 2 years.

Whereas the meningeal reaction during the acute stage is always infiltrative and exudative, the process of healing is of proliferative and productive character, with the formation of a specific granulation tissue rich in giant cells, followed by the development of sclerotic scar tissue on the meninges. This productive process in the central nervous system is dangerous in that it may cause irreversible changes in the vascular system and prevent the free circulation of cerebrospinal fluid. Moreover, during the process of healing exacerbations of meningitis are not uncommon. Chronic tuberculous meningitis may take any of the following forms: (1) Chorio-ependymitis, diffuse or circumscribed, often complicated by hydrocephalus of varying degree. (2) Meningo-vascular changes, especially frequent in more chronic forms. These may be subdivided into diffuse arteritis and phlebitis, endarteritis, and thrombosis. The symptoms depend on the site of the lesions. (3) Chronic leptopachymeningitis, diffuse or circumscribed, with clinical symptoms depending on the site. (4) Solitary or multiple tuberculomata with corresponding focal signs. (5) Caseation of brain, more frequently occurring in the subacute stage, with corresponding focal signs. *W. Szaynok*

1130. **Benign Meningeal Reactions following Recovery from Tuberculous Meningitis.** (Reazioni meningee benigne in pazienti guariti da meningite tubercolare)
P. NICOLAJ. *Clinica Pediatrica* [*Clin. pediat., Bologna*] **34**, 103–110, Feb., 1952. 1 fig., 8 refs.

The author presents the cases of 6 children who had been discharged from hospital cured of tuberculous meningitis by streptomycin therapy. All had a subsequent attack of headache, vomiting, and meningism with changes in the cerebrospinal fluid. The interval between discharge and the attack varied from 11 days to 22 months. Some patients had fever, and all had a raised level of albumin in the cerebrospinal fluid (0·66 to 1·33 g. per 100 ml.) with a positive Pandy reaction and leucocytes up to 500 per c.mm. Culture of the fluid for tubercle bacillus was negative in all cases. The symptoms subsided rapidly and the cerebrospinal fluid returned to normal in 2 to 3 weeks, both in the 3 cases that were given another course of streptomycin and in the 3 others that had no therapy.

The author considers that the most likely explanation for the meningism is an allergic response to the reactivation of a tuberculous focus, especially one which is adjacent to the meninges. One of the cases showed the meningeal reactions during an allergic response to eating strawberries. It is possible, however, that the patients were suffering from a mild benign lymphocytic meningitis. As the condition cannot, in its presenting symptoms, be distinguished from a recrudescence of tuberculous meningitis it is recommended that streptomycin therapy should be started at once. *Donald McDonald*

1131. **The Development of Measles during the Treatment of Tuberculous Meningitis with Streptomycin.** (Die Wirkung der Masern auf die in Streptomycinbehandlung befindliche Meningitis tuberculosa)
A. AKKOYUNLU. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **7**, 180–184, April, 1952.

The author describes 5 cases of tuberculous meningitis in which, during treatment with streptomycin, measles developed in a modified form. He concludes that streptomycin has an inhibitory effect on the growth of the measles virus, and recommends the prophylactic treatment with streptomycin of children with tuberculosis who have been in contact with measles, an attack of which is liable to aggravate the tuberculous condition.
Franz Heimann

Venereal Diseases

1132. **The Ito Skin Test for Chancroid in the Adult and Juvenile African**
R. R. WILLCOX. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **36**, 284–288, May, 1952. 5 refs.

The Ito, Reenstierne, or " dmelcos " reaction for the diagnosis of chancroid consists in the intradermal injection of a vaccine of Ducrey's bacillus, a positive reaction being demonstrable as a palpable button at 48 hours. The test is of little value in the diagnosis of the individual case in districts where the disease is rife, as 8 to 24 days must elapse after the appearance of the sore before a positive reaction can be obtained, and once the patient has become sensitive to the vaccine he may remain so for life. It is also suggested that the sensitive skin of an infant may give a false positive reaction and that the infant may inherit specific sensitivity from the mother. The main value of the test seems to be as a rough guide to the general incidence of the disease.

The test was performed on 1,022 African negroes, 990 in Southern Rhodesia and 32 in the Gold Coast, about 50% being patients at venereal disease clinics. The results indicate that the incidence of chancroid amongst Africans is high and that, like other venereal diseases, it is more prevalent in the towns, especially among the female prostitute population. *Neville Mascall*

LYMPHOGRANULOMA VENEREUM

1133. **A Five-year Study of Antibiotics in the Treatment of Granuloma Inguinale**
R. B. GREENBLATT, W. E. BARFIELD, R. B. DIENST, R. M. WEST, and M. ZISES. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **36**, 186–191, March, 1952. 26 refs.

This study of the use of antibiotics in the treatment of lymphogranuloma venereum was made at the Medical College of Georgia during 1946–51. Streptomycin was given intramuscularly in varied doses in order to establish an optimal therapeutic regimen; this was found to be 4·0 g. daily for 5 days. Of 142 patients treated with streptomycin, of whom 115 were followed up, only 14 required re-treatment but 8 of these proved to be streptomycin-resistant. Eighth-nerve involvement was not encountered, although several patients had pruritus with or without urticaria.

Aureomycin was given to 71 patients. The optimum oral dose was found to be 2 g. daily for 10 to 20 days, although a more prolonged regimen was found necessary in patients with extensive lesions. Of the 66 patients followed up, 11 required re-treatment; there were no cases of resistance to the drug. Toxic effects were few and mild and consisted of nausea, vomiting, and pruritus of the anus and vulva. Chloramphenicol was used in the treatment of 46 patients, and 2 g. daily for 10 to 20 days, or longer in extensive cases, was likewise found to be the optimum course; 42 patients were followed up and 10 required re-treatment; one case of resistance was noted. A few patients suffered from mild nausea or dermatitis.

The same optimum dosage was found in respect of terramycin, which was used for 36 patients, of whom 27 were followed up for periods up to one year; 2 patients have so far required re-treatment and there have been no failures. Mild nausea and headache were noted by 2 patients, but in none did the treatment have to be discontinued. Although oral therapy may be given to outpatients, treatment in hospital under supervision is considered desirable. *R. R. Willcox*

SYPHILIS

1134. **Therapy of Early Syphilis with Penicillin Administered by Jet Injection**
A. L. WEINER, R. H. PRESTON, and W. SNYDER. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **18**, 327–332, April, 1952. 2 figs., 8 refs.

Jet injections are administered by means of the " hypospray ", which delivers the material to be injected through a fine jet at sufficiently high pressure to ensure penetration through skin and subcutaneous tissue to muscle without the aid of a needle. The present authors support the claims of the originators of this technique that it is effective and relatively painless, having special advantages in the treatment of children and " needle-shy " adults. It may also be of value in lessening contamination of the skin with a preparation to which the patient may be hypersensitive and in avoiding dissemination of the causative organism of infective hepatitis.

This report concerns the use of jet injections of a preparation of procaine penicillin in sesame oil with 2% aluminium monostearate (PAM) in the treatment of early syphilis. In order to determine whether the blood levels of penicillin were satisfactory when the drug was given in this way, 10 patients, not all of whom were suffering from syphilis, were each given an injection of 300,000 units of PAM, first by means of a needle and then, after the lapse of not less than one week, by hypospray; the blood levels of penicillin were determined 4, 12, 24, and 48 hours after each injection. These levels showed some variations from patient to patient, but no significant differences as between the two techniques of injection. The hypospray was then used in the treatment of 67 patients with various types of early syphilis, most of them receiving 9 daily injections each of 300,000 units of the drug, giving a total dosage in each case of 2·7 mega units. The healing of syphilitic lesions, the disappearance of

treponemes from the secretion, and the reversal of serological reactions in these cases followed a similar course to that commonly found with the same preparation given in the normal way.

There were only 3 cases in which the treatment failed, 45 of the patients being followed up for 3 to 17 months and 31 for more than 6 months. Five patients were treated for syphilis during pregnancy by this method, and all were delivered of healthy children. Reactions to treatment were few: only 6 Jarisch–Herxheimer reactions were observed, a number which is considerably below what might be expected. One patient developed a generalized papulo-vesicular eruption after the sixth injection.

The authors make no claims for this method of treating syphilis, but consider that the evidence presented suggests that it gives rise to no loss of efficacy. *A. J. King*

1135. **A Comparison of Current Methods of Treatment of Syphilis.** (Nos expériences dans le traitement actuel de la syphilis)
N. BARYAKTAROVITCH and R. DAMJANOVITCH. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **79**, 30–40, Jan.–Feb., 1952. 1 fig., 21 refs.

In 100 cases of primary or secondary syphilis treated at the Dermato-Venereological Clinic of the University of Belgrade, the authors employed 4 methods: penicillin alone, by injection or by mouth; penicillin–bismuth; penicillin–arsenic; and penicillin–arsenic–bismuth. The results were compared, in respect of speed of disappearance of *Treponema pallidum*, speed of disappearance of lesions, and speed of serological reversal, with those obtained with arsenic and bismuth.

As regards serological reversal, it is concluded that the results of treatment with penicillin alone are not inferior to those of arsenic–bismuth or bismuth, and are superior when the antibiotic is associated with arsenic or bismuth, while from the bacteriological and clinical points of view penicillin, especially when combined with bismuth, gives better results than were obtainable by the older methods of treatment. The authors found penicillin to be as effective given by mouth as by injection.

James Marshall

1136. **The Provocative Serological Reaction in Late Syphilis: its Relation to Technical Factors**
R. W. MAXWELL and V. SCOTT. *Annals of Internal Medicine* [*Ann. intern. Med.*] **36**, 979–991, April, 1952. 21 refs.

The authors, at Washington University, St. Louis, report the results of serial quantitative Kahn and V.D.R.L. slide flocculation tests on 12 previously untreated patients with late syphilis, of whom 10 had neurosyphilis with seropositive cerebrospinal fluid, one a gumma of the nasal septum, and one late latent syphilis. To give a base-line for comparison of titres 2 to 4 specimens of serum were obtained before treatment, then on alternate days of the first week of treatment and once weekly for the next 3 to 4 weeks. Each specimen was divided into two parts, one being examined at once and the other kept at −70° C. until the series of specimens was complete and all could be examined simultaneously. " Provocative " treatment consisted of " mapharsen ", 0·001 g. per kg. body weight followed by bismuth subsalicylate in oil (4 patients) or water-soluble thiobismol (5 patients) once weekly for 3 to 4 weeks. Three patients were treated with 600,000 units of procaine penicillin in oil twice weekly for 3 to 4 weeks.

The serial titres obtained with the fresh sera showed considerable variation, more marked with the Kahn than with the V.D.R.L. antigen and greater in the sera with high than those with low titres. A more stable series of titres was obtained with the frozen sera, the mean variation for the 12 patients being 2 dilutions with the Kahn and one dilution with the V.D.R.L. test; the corresponding figures for the fresh sera were 3 and 2 dilutions respectively. No evidence of a provocative effect was obtained. An apparent rise in titre was found at some stage in 3 cases when the fresh sera were examined with one test but not with the other. No such rise in titre was found with either test when the frozen sera from these patients were examined. The variations in titre are thought to be due to day-to-day fluctuations in the sensitivity of the tests used. [It is not stated whether antigens of the same batches were used throughout the investigation.] *A. E. Wilkinson*

1137. **Interpretation of Serum Reactions in Late Syphilis**
C. P. HEYWOOD. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **28**, 3–12, March, 1952. 4 figs., 18 refs.

The author discusses the behaviour in late syphilis of the serological reactions, and their relation to the diagnosis and treatment of the condition. He points out that present-day serological tests are both highly sensitive and highly specific, and concludes that " with appropriate safeguards to exclude temporarily false positive reactions, a positive reaction means that the patient has been infected with syphilis at some time in his life ". Also that a very rough indication of the age of the infection [presumably only in relation to the later stages of syphilis] is provided by a quantitative serological test, as a positive reaction to a high titre indicates a more recent infection, while a positive reaction to only a low titre indicates an infection of longer duration because of the tendency towards spontaneous reversal with the passage of time.

The significance of a persistently positive reaction in an adequately treated patient in the absence of all other evidence of the disease is problematical, for until the source of the reagin is definitely known it is impossible to decide whether the reaction arises from a focus of treponemes sealed off from the influence of treatment or whether it is due to a permanent metabolic change in tissue previously infected with syphilis but no longer harbouring the organisms. As the ultimate clinical fate of seroresistant patients cannot be judged from their serological reactions, these tests are not a guide to treatment. Moreover, the author concludes, the treatment of late syphilis should not be expected to produce a negative serology, and attempts to achieve this aim are doomed to failure. *T. Anwyl-Davies*

Tropical Medicine

1138. **Terramycin in Cholera**
A. DAS, S. GHOSAL, S. K. GUPTA, and R. N. CHAUDHURI. *Indian Medical Gazette* [*Indian med. Gaz.*] **86**, 437–444, Oct., 1951. 1 ref.

It is recalled that chloramphenicol will cause rapid disappearance of vibrios from the faeces of patients with cholera; this does not make any difference to the clinical course of the disease, which depends mostly on the dehydration of the patient and responds only to the parenteral administration of fluid. Similar investigations have now been carried out with terramycin. Preliminary experiments showed that growth of *Vibrio cholerae* is inhibited *in vitro* by 2 to 5 μg. of terramycin per ml.

Of 72 patients aged 7 to 68 years admitted to hospital (27 males and 45 females), 36 (alternate patients) were given terramycin and the other 36 were used as controls. Apart from administration of terramycin the treatment of the two groups was identical. The antibiotic was given orally in capsules, 1 g. on admission, 0·5 g. after 2 hours, and then 0·5 g. every 6 hours till the end of the third day, the total dose being 6 to 7 g. Cholera vibrios were isolated from the stools of 29 of the 36 patients given terramycin, and from 23 of the 36 controls. Terramycin had no obvious effect on the clinical course of the disease. There were 6 deaths in the treated group and 8 in the control group. Bacteriologically, however, the results were striking. In the treated group the faeces were free from vibrios by the second day, while in the control group the faeces of one man out of 17 still contained vibrios on the sixth day. This rapid clearance may be advantageous from the public health point of view.

F. Hawking

1139. **Immunization Against Scrub Typhus: Duration of Immunity in Volunteers following Combined Living Vaccine and Chemoprophylaxis**
J. E. SMADEL, H. L. LEY, F. H. DIERCKS, P. Y. PATERSON, C. L. WISSEMAN, and R. TRAUB. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **1**, 87–97, Jan., 1952. 14 refs.

Human volunteers, most of whom had had previous rickettsial infection, were used in these immunization experiments. The strains of *Rickettsia tsutsugamushi* tested were the Gilliam, the Karp, and C.P.14. The inoculum was lyophilized vaccine, rehydrated and diluted in saline containing 10% inactivated serum from an individual who had suffered from neither scrub typhus nor infective hepatitis; 0·1 ml. was given intradermally, the dilution being controlled by titrations in mice. There was no difference between the immunity resulting from an overt attack of scrub typhus (promptly controlled by chloramphenicol) and that resulting from complete suppression of development of the disease. Immunity to the homologous strain of *Rickettsia* persisted at a high level in most persons for at least a year, and in some for longer periods.

Resistance to infection with heterologous strains of *R. tsutsugamushi* was of a transient nature. Partial immunity can prevent the appearance of the local primary lesion even though the generalized disease occurs. Even within one month after inoculation with one strain an appreciable number of persons became ill following injection with a heterologous strain. By the end of a year, all were again susceptible to heterologous infection. During the period of waning immunity the clinical picture of the disease which resulted from the heterologous strain was modified from the classical picture. Indeed, the illness observed in the test shortly after recovery was so mild that it would probably not have been recognized as scrub typhus if rickettsaemia had not been demonstrated. On the other hand, the disease which resulted when the individuals were tested after one year generally presented the typical picture of scrub typhus.

W. H. Horner Andrews

PROTOZOAL INFECTIONS

1140. **Liver Function Studies in Malaria—I**
P. N. WAHI and M. M. ARORA. *Indian Journal of the Medical Sciences* [*Indian J. med. Sci.*] **6**, 165–176, March, 1952. 2 figs.

The literature contains few reports of liver function studies in naturally acquired malaria, and fewer still in which more than one function test has been applied. The authors have tried to evaluate hepatic dysfunction in 50 acute and 60 chronic cases of naturally acquired malaria. Of the 50 cases of acute malaria the result of the thymol turbidity test was positive in 7, while that of the thymol flocculation test was positive or probably positive in 19. The colloidal gold flocculation reaction was positive in 13 cases, 2 of which were negative to both thymol tests. The colloidal gold and thymol flocculation tests appeared to be about equally sensitive, although the overlap was incomplete. The cephalin–cholesterol flocculation test was carried out 24 and 48 hours after the onset of the disease. At 48 hours 37 of the cases gave a positive reaction. Again overlap with the other tests was incomplete, and 4 cases negative to this test were positive to the other flocculation tests. In one case there was a positive reaction to the gold test only.

In 32 cases the retention of bromsulphalein was greater than 2·5% 30 minutes after an injection of 5 mg. per kg. body weight. The total bilirubin content of the serum was over 0·6 mg. per 100 ml. in 7 cases. Urobilinogen was detected in the urine in one case only, at a dilution of 1 in 40. The total plasma protein level was less than 5·98 g. per 100 ml. in 17 out of 30 cases, and that of albumin was below 3·6 g. per 100 ml. in 25. There

was a "slight to significant" increase in the plasma globulin level (normal 2·2 g. per 100 ml.) in 13 of these 30 cases.

Summarizing, in 5 of the 50 cases no evidence of liver dysfunction was given by any test; in 45 there was a positive reaction to one or more of the tests; and in 18 there was a positive reaction to one test only, the nature of which varied. The authors state that the nature and extent of the functional derangement were independent of the species of infecting *Plasmodium*, the number of rigors, or the duration of acute attacks.

W. H. Horner Andrews

1141. **Liver Function Studies in Malaria—II**
P. N. WAHI and M. M. ARORA. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **6**, 235–245, April, 1952. 2 figs., bibliography.

In this paper the authors report the results of liver function tests in 60 cases of chronic relapsing malaria. [For the results in 50 acute cases see Abstract 1140.] The result of the thymol turbidity test was positive in 40 of these 60 cases; that of the thymol flocculation test was positive in 44 cases and negative in 1 case in which a positive result had been obtained with the turbidity test. In contradistinction to the findings in acute malaria both thymol tests appeared to be equally sensitive. The reaction to the colloidal gold flocculation test was positive in 41 cases, 38 of which were positive to both thymol tests. The result of the cephalin–cholesterol test was "definitely positive" in 47 cases and "strongly suspicious positive" in a further 10: the overlap with the other tests was not quite complete.

In 54 cases retention of bromsulphalein was greater than 5%; this test was the only one to give a positive result in one of the patients. The total bilirubin content of the serum was above 0·6 mg. per 100 ml. in 19 cases, and the urobilinogen level in the urine was within normal limits in all but 2. In 20 of the 40 patients tested there was some degree of hypoproteinaemia, and in 38 hypoalbuminaemia. The plasma globulin level was raised in 31. The prothrombin time was assessed in 43 cases, and was found deficient in 35; in general the response to vitamin K was poor.

Only in one case were negative results obtained with all the tests, the majority giving positive results to 5 or 6 tests. There appeared to be no correlation with the type of infecting *Plasmodium*, the number of relapses, or the duration of attacks.

The authors emphasize the value of a series of tests in assessing liver damage, especially in acute malaria. They suggest that malaria may give rise to permanent liver damage, and in the present work have attempted by means of needle biopsy to exclude any hepatic condition other than that due to malaria.

[Although these are valuable papers, they are marred by the absence of such details as the number of cases of each type of malarial infection. It is difficult, too, to reconcile the statements that "permanent liver damage ultimately results", and that the frequency and duration of relapses "had no effect on the extent of the liver damage". Also as the findings in acute and chronic malaria are shown to differ, this last statement appears rather inapt. Moreover, the cephalin–cholesterol flocculation test was positive in more patients after 48 hours than after 24.] *W. H. Horner Andrews*

1142. **Treatment of Chronic Intestinal Amebiasis with a New Oxyquinoline Compound**
H. WENGER. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **6**, 246–249, April, 1952.

Trials have been carried out in India of 5:7-dichlor-8-hydroxyquinaldine in the treatment of infections with *Entamoeba histolytica*, usually of a chronic type. In 26 cases the information available was sufficiently complete for conclusions to be drawn as to the result. The usual dose was 0·2 g. twice daily by mouth for 4 to 5 days (the patients' average weight being two-thirds of that of Europeans). *E. histolytica* was present in the faeces in all cases before treatment. After treatment neither amoebae nor cysts could be found in the faeces in 12 cases on one examination, in 10 cases on 2 examinations, and in 4 cases on 3 examinations. In one case, severe amoebic hepatitis persisted in spite of treatment (although the stools were cleared), and emetine was required. There were no side-effects. *F. Hawking*

NUTRITIONAL AND METABOLIC DISORDERS

1143. **The Heart in Chronic Malnutrition**
J. HIGGINSON, A. D. GILLANDERS, and J. F. MURRAY. *British Heart Journal* [*Brit. Heart J.*] **14**, 213–224, April, 1952. 10 figs., 35 refs.

A form of heart disease has been observed among the Bantu population which, the authors suggest, is due to chronic malnutrition. The patients have a poor nutritional background and suffer from recurrent attacks of congestive heart failure, the first attack of which responds to a good diet, but not to aneurin alone. A poor diet results in relapses and, usually, sudden death in failure. The findings at necropsy, which was carried out in 12 cases, were those of chronic heart failure, with serous effusions and adhesions, ventricular thrombi and peripheral emboli, and varying degrees of primary liver disease and haemosiderosis. *Marjorie Le Vay*

1144. **Some Observations on the Diet of Jamaican Children, with Particular Reference to Liver Disease**
K. RHODES. *British Journal of Nutrition* [*Brit. J. Nutrit.*] **6**, 198–206, 1952. 3 figs., 18 refs.

The author, working in Jamaica, has studied the liver disease which affects local children, and reports the results of a dietary survey in these cases. The affected children do not appear ill-nourished, though they are stunted in growth compared with controls. They are pot-bellied, owing to a large liver and, sometimes, to splenomegaly and ascites. Biopsy examination of the liver shows oedema of the perisinusoidal spaces in the early stages, later an eosinophilic coagulum, and finally cirrhosis.

The diet of a group of 10 children with liver disease and a group of 5 normal children was investigated. The

ages of the children ranged from 9 months to 8 years and none had been breast fed. Dietary intake was measured in the patient's home for 4 to 7 days in each case. The normal standard intake of protein was taken as 3·5 g. per kg. body weight, and on this basis it was found that the average protein intake of the children with liver disease was 32·5% of normal, with a range of 13% to 52·5%, compared with 72·5%, with a range of 60% to 78%, for the healthy children. The average intake of fat was also higher in the healthy children, but carbohydrate intake was about the same in both groups. The diet of the healthy children contained a much higher percentage of animal protein than did that of the children with liver disease, and the sources of the protein were more varied. The survey also showed that the children with liver disease not only had a monotonous diet which was deficient in animal protein, but also consumed an excess of refined carbohydrate foods. The author considers that inadequate diet, especially the protein deficiency, is the chief cause of the liver disease. Some success in treatment has been achieved with administration of a protein concentrate. *William Hughes*

1145. **Pancreatic Enyzme Activity in Duodenal Contents of Children with a Type of Kwashiorkor**
M. D. THOMPSON and H. C. TROWELL. *Lancet* [*Lancet*] **1**, 1031–1035, May 24, 1952. 4 figs., 19 refs.

The malnutritional condition in children which was first described in 1933 under the name of kwashiorkor has remained a not very clearly defined syndrome, although it is recognized among the indigenous inhabitants of a large part of the tropical world. The aetiology likewise has remained undetermined, though a protein deficiency probably plays a part and there is some evidence in favour of a failure of digestion or of absorption.

The investigation described in this paper was undertaken to determine whether pancreatic function in kwashiorkor is normal. The authors estimated the pancreatic enzyme activity (amylase and lipase) of the contents of the duodenum, obtained by intubation and aspiration, in 40 children aged 12 to 51 months before and after treatment and in a further 19 children on admission only; 24 children under treatment for other conditions formed a control group.

The concentration of amylase and lipase in the controls varied widely, but the mean was higher than in the children with kwashiorkor. After the 40 children had been treated there was again a very wide variation in concentration, but the mean was about the same as in the control group. The wide range of variation in the values for enzyme activity is ascribed to the number of variables involved in the technique of collection, but the authors infer from the parallelism of the concentrations of the two enzymes that the picture is a correct one. They also infer that the trypsin concentration would follow the same trend. This appears to be justified, because the results of investigations in 3 further cases showed a depression of the concentration of trypsin comparable to that observed for amylase and lipase. Enzyme activity returned to normal levels within 1 to 7 weeks when the patients were given milk or milk-protein supplements to the standard hospital diet, together with treatment for any active infection (malaria, hookworm).

This reversible depression of pancreatic-enzyme activity appears to find a counterpart in the histological changes in the pancreas in untreated cases, when there is an absence of zymogen granules and of cytoplasm around the nucleus. The authors suggest that depressed pancreatic activity interferes with digestion in the small intestine and thus reduces the absorption of protein.
H. S. Stannus

1146. **Criteria for Assessing Fat Absorption in Normal Subjects and Sprue Patients**
C. F. ASENJO. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop Med. Hyg.*] **1**, 344–354, March, 1952. 26 refs.

The absorption and excretion of fat were studied in 41 patients with sprue and 19 normal subjects. The estimation of the percentage fat content of the stools was found to be an unsatisfactory method of evaluating fat loss. Balance studies showed an average fat absorption of 94% in normal subjects and 60% in the patients with sprue. In the latter the proportion of split fat was slightly greater than normal, that of neutral fat the same, and that of unsaponifiable matter about half the normal value. *A. C. Frazer*

1147. **The Comparative Effect of Vitamin B_{12} Administered through Different Routes in Tropical Sprue.** [In English]
R. M. SUAREZ. *Internationale Zeitschrift für Vitaminforschung* [*Int. Z. Vitaminforsch.*] **23**, 308–318, 1952. 6 figs., 2 refs.

The author reports his experience in cases of tropical sprue of administering vitamin B_{12} intramuscularly, orally, sublingually, or by instillation into sternal marrow. He found that intramuscular injection was the most effective method of administration, 100 μg. being generally adequate, with a maintenance dose of 15 μg. weekly. Neurological signs disappeared and no fresh involvement of the nervous system was observed during treatment. A more sustained effect was obtained with a single intramuscular injection of 100 μg. than with 10 injections of 10 μg. daily or at intervals of a few days. In 2 patients who received a single injection of 1,000 μg. there was maximum and sustained improvement in the clinical condition and in the blood picture. A good response was obtained with oral administration of 3,000, 5,000, or 10,000 μg., but the results were less predictable. The effective oral dose was probably 200 times greater than the effective intramuscular dose. Sublingual administration was unsatisfactory in doses of 25 μg. for 10 consecutive days. As regards the introduction of vitamin B_{12} directly into the bone marrow, the author considers that the theory of Horrigan and Vilter that in pernicious anaemia vitamin B_{12} is taken up by cells at the site of injection holds good also for sprue, the maturation effect of such injections being less marked in distant bone marrow. *R. Crawford*

Allergy

1148. **Stress Studies in the Eczema–Asthma–Hay-fever Diathesis**
T. H. STERNBERG and M. C. ZIMMERMAN. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **65**, 392–400, April, 1952. 4 figs., 5 refs.

A comparison was made between the eosinophil counts of 22 control cases and 27 cases of atopic dermatitis under conditions of rest, after an injection of adrenaline, and after exposure to stress. The patients in the latter group all had clinically typical atopic dermatitis with a history of at least 3 years; many also had asthma, hay-fever, or " hives ". The controls were of comparable age and had no history of any allergic disease. The eosinophil counts were carried out on 3 separate non-consecutive days at 8 a.m. and again at 12.15 p.m. On the rest days the patients and controls read or relaxed between the two readings; on " adrenaline days " adrenaline was injected subcutaneously in a dose of 0·01 mg. per kg. body weight immediately after the 8 a.m. specimen of blood had been taken, and patients then read or relaxed till 12.15 p.m.; the stress situation consisted of exposure to a temperature of 100° to 115° F. (37·8° to 46·1° C.) and 85 to 90% humidity for one hour immediately after the morning specimen had been taken; after leaving the hot room the subjects were allowed to have a shower bath and to rest till noon.

The normal and control groups showed no statistical difference under conditions of rest or after adrenaline. There was no appreciable change in the eosinophil count after rest alone; after adrenaline both groups showed a well-marked eosinopenic response. After exposure in the hot room the two groups differed in their response, the atopic subjects failing to develop eosinopenia; this difference was of high statistical significance. Individual exceptions were noted, however, in both the control and atopic groups. When the lymphocyte–neutrophil ratio was examined under the same conditions both groups showed a lowered ratio (that is, development of lymphopenia and a neutrophilic leucocytosis) after adrenaline and stress, though the average fall was less in the atopic group. The individual variation within both groups was wide.

It is concluded that though atopic subjects are capable of responding normally through the pituitary and adrenal cortex to the stimulus of exogenous adrenaline, they do not do so when exposed to a standard stress situation. No conclusion can be drawn as to whether the failure in this group of cases lies in the higher brain centres, the hypothalamus, or the adrenal medulla.

[Evidence is accumulating to show that the fall in the number of eosinophil leucocytes after adrenaline, or other drugs such as salicylates, is not directly mediated through the pituitary and adrenal glands, and that this conception is almost certainly an over-simplification.]

R. S. Bruce Pearson

1149. **The Clinical Physiopathology of Asthma.** (Physiopathologie clinique de l'asthme)
R. KOURILSKY, S. KOURILSKY, G. DECROIX, J. A. GENDROT, and A. MIGNOT. *Annales de Médecine* [*Ann. Méd.*] **53**, 138–171, 1952. 5 figs., bibliography.

The authors have followed the course of chronic asthmatic disease in 50 patients for a period of 5 to 10 years. They come to the conclusion that three main factors are concerned in the aetiology of asthma: a nutritional factor, a psychological factor, and an infective factor. If these three causes are removed, therapeutic success can be achieved in 95% of cases without recourse to anti-allergic or symptomatic treatment; without their removal or modification no lasting therapeutic success is possible.

The nutritional factor was present in more than 75% of the cases: milk, cheese, cream, eggs, certain fats, and sometimes the leguminous plants were all incriminated, and their removal from the diet improved even cases with a long history. The psychological factor also requires treatment. It is admitted that in infectious asthma the connexion between allergic disposition and chronic infection makes treatment difficult. Of their 50 cases the authors claim 12 as cured, 27 as improved, and 8 as unimproved; 4 patients died [this gives a total of 51. No case histories or any other details of the cases or their treatment are given]. A number of photomicrographs of bronchial biopsies are reproduced showing inflammatory lesions of mucosa and submucosal tissue.

H. Herxheimer

1150. **Cortisone in Asthma**
H. S. MITCHELL and G. CAMERON. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **66**, 313–316, April, 1952. 7 refs.

Cortisone, with or without corticotrophin, was given to 21 patients, 4 females and 17 males, suffering from severe intractable asthma. The cortisone was given intramuscularly or orally in doses of 200 to 300 mg. for 2 days, followed by 100 mg. daily, and later by 50 mg. a day. There was marked improvement in 9 patients, slight improvement in 5, and no improvement in 7. Of the 9 patients showing marked improvement 4 obtained complete subjective and objective relief of symptoms, 2 of these having been given corticotrophin for the first 2 days with cortisone. Most of the patients who did not respond had severe emphysema and chronic bronchitis of long standing. The response was observed in 24 hours to 6 days after the treatment started, the maximum benefit being obtained within 3 to 9 days except in 2 cases, when the maximum benefit was observed as late as the 12th and 17th days respectively. Relapses occurred 1 week to 3 months after treatment was stopped. Three patients in status asthmaticus responded dramatically to cortisone.

J. Pepys

Gastroenterology

OESOPHAGUS

1151. **Recent Advances in the Construction of an Artificial Oesophagus.** (Новое в создании искусственного пищевода)
B. A. Petrov and G. R. Chundadze. *Хирургия* [*Khirurgiya*] 3–14, No. 2, Feb., 1952. 10 refs.

The authors review their recent experience in the construction of an artificial oesophagus. From 1949 to 1950, 123 such operations were performed at their hospital, 110 of the patients suffering from oesophageal stricture following burns and the remaining 13 patients having previously undergone oesophagectomy for carcinoma. In all cases the small intestine was used. The antethoracic route was chosen in all except 7 cases in which it was possible to anastomose the jejunum to the oesophagus within the pleural cavity. Only 9 patients died—7 after antethoracic and 2 after intrathoracic anastomosis. Only in one case was a fault in technique responsible for necrosis of the mobilized intestine and death, the other patients dying from causes unrelated to the operation.

The improvement in results during the last few years has been due to the measures adopted to increase the length of the mobilized segment of intestine and to improve its blood supply. For these purposes the authors mobilize the root of the mesentery by stripping the posterior abdominal wall of its peritoneal covering. If the viability of the intestine appears to be in danger, they perform an anastomosis between the internal mammary or gastro-epiploic artery and one of the main branches supplying the mobilized loop of gut.

Z. W. Skomoroch

1152. **Arterial Anastomosis as a Means of Improving the Blood Supply of the Intestinal Graft in the Construction of an Artificial Oesophagus.** (Сосудистое соустье как метод добавочного кровоснабжения кишки при создании искусственного пищевода)
P. I. Androsov. *Хирургия* [*Khirurgiya*] 15–22, No. 2, Feb., 1952. 3 figs., 8 refs.

The author describes a technique of construction of an artificial oesophagus in which arterial anastomosis is used to improve the blood supply of the mobilized segment of small intestine. Goudov's apparatus was used for the vascular anastomosis. In 5 patients the right gastro-epiploic artery was anastomosed to the fourth main branch supplying the mobilized gut, and in a number of others the left internal mammary artery was anastomosed with the second mesenteric branch. The functioning of the anastomoses was demonstrated by arteriography.

Illustrative case histories are given and the technique is described in great detail. *Z. W. Skomoroch*

STOMACH

1153. **The Relation of Gastric Secretion to Events following Pyloric Obstruction**
J. S. Clarke, H. A. Oberhelman, S. O. Evans, and L. R. Dragstedt. *Annals of Surgery* [*Ann. Surg.*] **135**, 433–440, April, 1952. 26 refs.

For 20 years it has been recognized that the chief cause of death in simple high bowel obstruction is loss of water and electrolytes, and that the administration of normal saline delays death. Normally, secretions originating proximal to the pylorus are re-absorbed in the intestine so that the body's extracellular fluid reservoirs are kept constant, but in pyloric obstruction these fluids lie in the stomach or are vomited and are unavailable to the organism. The rate of loss of water and inorganic ions, and therefore the length of survival, depends on the rate at which they are transferred from the tissue fluids into the lumen of the stomach. In experiments carried out at the University of Chicago on dogs the authors found that the drinking of water in the presence of pyloric obstruction increased the diffusion of water and chloride into the stomach and so increased their loss, the large volume of hypotonic fluid lying in the stomach causing a passive diffusion of electrolytes from the relatively hypertonic extracellular fluids into the gastric lumen. Similarly, large volumes of saline or glucose solution given parenterally increased the secretion into the stomach. On the other hand vagal resection, or antral resection, or the drinking of normal saline diminished the rate of gastric secretion, and so prolonged life, and there was some evidence that some water was even absorbed from the stomach. It is possible that antral distension is an excitant of gastric secretion, which would explain the diminished loss of electrolytes after antral resection. *Norman C. Tanner*

1154. **Electrolyte Abnormalities in Pyloric Obstruction Resulting from Peptic Ulcer or Gastric Carcinoma**
H. S. Lans, I. F. Stein, and K. A. Meyer. *Annals of Surgery* [*Ann. Surg.*] **135**, 441–453, April, 1952. 29 refs.

It is now well known that in cases of pyloric obstruction with vomiting the loss of chloride and sodium are important factors in the production of the " toxaemic " condition of the patient. In a study of 24 cases of pyloric obstruction accompanied by vomiting or treated by gastric aspiration at the Cook County Hospital, Chicago, the authors found the serum potassium concentration in all cases to be below 3·5 mEq. per litre (normal 4·0 to 5·6 mEq. per litre), indicating a probable intracellular potassium deficiency. This hypokalaemia appears to be aggravated by the parenteral administration of fluids not containing potassium. It was found that a daily loss of 3 to 4 litres of gastro-intestinal secretion

contained potassium equivalent to 6 to 8 g. of KCl. In some cases of potassium deficiency the electrocardiogram may not be changed, and estimation of the serum potassium level is a more reliable index.

Clinically, the patients exhibited lethargy and mental depression; 7 were confused and 3 disorientated. Muscle weakness was present in all, one having paralysis of both lower limbs, while respiration was shallow and slowed in 8 cases. The institution of intravenous potassium therapy resulted in a striking improvement in the mental attitude and muscle power of all the patients. The authors recommend the addition of 3 g. of potassium chloride to each litre of isotonic sodium chloride used for intravenous infusion. Amino-acids or 5% dextrose may also be added. The solution should not be given more rapidly than 8 to 12 ml. per minute and frequent serum potassium estimations should be made, as a high serum potassium level may cause heart block or cardiac arrest. A total of 9 to 15 g. of potassium chloride should be given daily until the serum potassium level has been normal for 24 hours, after which a maintenance dose of 6 g. daily will suffice. Most foods are good sources of potassium, and the dose may therefore be discontinued as soon as the patient can be fed by mouth. Caution is required in cases of renal insufficiency or dehydration.

Norman C. Tanner

1155. **A Study of the Morphological Factors Associated with Survival for More than Five Years after Operation for Carcinoma of the Stomach.** (Studio dei fattori morfologici connessi con la sopravvivenza oltre i 5 anni dall'intervento nel carcinoma gastrico)

L. Tonelli and G. Favacchio. *Policlinico, Sez. Chirurgica* [*Policlinico, Sez. Chir.*] **59**, 65–105, March–April, 1952. 29 figs., 21 refs.

From the Institute of Surgical Pathology of the University of Rome the authors present a study of the relation between histological appearance and clinical malignancy in gastric carcinoma. A distinctive type of carcinoma, similar to the carcinoids and of apparently low malignancy, was found in 7 out of 32 patients who survived 5 years or longer after partial gastrectomy. This type of growth did not occur among 32 patients who died within 18 months of operation. The authors do not think that the pathologist is justified in giving a prognosis as to expectancy of life based on the histological appearance of an excised gastric carcinoma unless this carcinoid-like growth is found, when the outlook is favourable.

N. Alders

1156. **New Anticholinergic Drugs in Peptic Ulcer Therapy**

N. Steinberg. *Review of Gastroenterology* [*Rev. Gastroent.*] **19**, 351–370, May, 1952. 3 figs., 22 refs.

Results are reported from the Community Hospital, Philadelphia, of the clinical trial in 40 patients with peptic ulcer of the atropine-like substances, "dibutoline" (di-*n*-butylcarbamylcholine chloride) and tropine benzohydryl ether methanesulphonate ("MK–02"). Atropine itself when used to reduce gastric activity frequently produces undesirable side-effects. Dibutoline has previously been used as a spasmolytic; for an inhibitory effect on the stomach it must be injected at frequent intervals. Tropine benzohydryl is chemically related to both atropine and to diphenhydramine ("benadryl").

Usually, except for patients with mild symptoms who received oral treatment only, an initial treatment for 2 or 3 days with 10 mg. of dibutoline subcutaneously every 3 hours was followed by 0·5 to 2 mg. of tropine benzohydryl orally every 6 hours. In 4 patients the initial treatment consisted of injections of tropine benzohydryl. Both substances gave rapid relief of the pain associated with peptic ulcer; nausea and vomiting stopped after the injection of dibutoline. [It is claimed that this was more effective than atropine, causing fewer side-effects, but the detailed table of results shows that only 3 patients received both atropine and dibutoline.] "Banthine" was equally as effective as tropine benzohydryl by mouth in "a number of cases", and occasionally was effective when the latter was not, or was causing undesirable side-effects; but generally tropine benzohydryl may be preferable to banthine as it has no bitter taste and in effective doses is cheaper than banthine. The best over-all results were obtained with tropine benzohydryl orally for 2 or 3 months, followed by treatment with antacids and diet. Tropine benzohydryl has toxic effects like those of atropine—blurring of vision, dry mouth, and dizziness—but causes no flushing or cardiac acceleration.

[From this report it appears that these substances are of value in the treatment of peptic ulcer. It is difficult, however, to assess their merits relative to atropine, as all cause side-effects in a proportion of cases.]

Derek R. Wood

1157. **The Effects of Partial Gastrectomy on Canine External Pancreatic Secretion**

D. Annis and G. A. Hallenbeck. *Surgery* [*Surgery*] **31**, 517–527, April, 1952. 5 figs., 14 refs.

The secretory response of the pancreas to the ingestion of a meat meal was studied in 5 dogs before and after partial gastrectomy. The pancreatic juice was collected by direct cannulation. In 2 dogs a Billroth-I type of operation was carried out, and in the other 3 partial resection with an anastomosis of the Polya type. The total bicarbonate and nitrogen content and the tryptic activity of the pancreatic juice were greatly reduced for 3 hours after a meat meal as a result of partial gastrectomy. In one dog no secretion occurred within 9 hours of the meal, but in the others some secretion started within 4 to 9 hours.

There was no alteration in the pancreatic activity in 3 dogs after operation for periods of 6 to 15 months; in the fourth dog observation extended over a period of one month only; in the fifth animal secretion returned to normal after 3 to 4 weeks. Only half of the stomach had been resected in the fifth dog, but after removal of a further part of the stomach to make the animal comparable with the others there was a similar transient effect. In all the animals the pancreas responded normally after operation to stimulation with secretin or

acid. Delayed emptying of the gastric remnant was observed in only one of the dogs.

The possible factors concerned in these effects on pancreatic secretion are discussed. *A. C. Frazer*

1158. **Incidence and Mechanism of the Early Dumping Syndrome after Gastrectomy. A Clinical and Radiological Study**
J. C. GOLIGHER and T. R. RILEY. *Lancet* [*Lancet*] **1**, 630–636, March 29, 1952. 9 figs., 25 refs.

In this paper from St. Mary's Hospital, London, is described the radiological investigation of 224 cases in which gastric resection in various degrees had been performed 6 months earlier. An attempt is made to correlate the findings with postprandial discomfort and the size of meal which could be taken.

The following findings are noteworthy: (1) the smaller the gastric remnant the more frequent the symptoms; (2) the rate of gastric emptying is unaffected by the type of operation (including Billroth-I and valve gastrectomies); and (3) the incidence of symptoms, which were thought to be caused by distension of the upper small bowel, is not related to the filling of the proximal loop. The total incidence of severe symptoms was 12·5% at 6 months and 7·1% at 18 months.

J. Marshall Pullan

1159. **Gastritis: a Study of 112 Cases Diagnosed by Gastric Biopsy**
R. K. DOIG and I. J. WOOD. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 593–600, May 3, 1952. 1 fig., 24 refs.

The authors present a study of 112 cases, seen at the Royal Melbourne Hospital, in which the diagnosis of "gastritis" was made on histological grounds from fragments obtained with a flexible gastric-biopsy tube. The cases were divided into: (1) "superficial" gastritis, where atrophy of the glands affected less than half the normal complement of specific cells; (2) "atrophic" gastritis, where the atrophy affected more than half the normal.

No single aetiological factor was found, although there were 19 patients with chronic alcoholism in the whole group. The usual symptom was epigastric discomfort half an hour after meals, which in some cases was relieved by alkalis. Nocturnal pain did not occur, but occasional nausea, vomiting, or diarrhoea was observed. Abdominal tenderness, atrophy of the tongue, and anaemia were the most frequent physical signs; 4 patients with superficial gastritis and 2 with atrophic gastritis were admitted to hospital because of haematemesis or melaena. The gastroscopic findings bore no relation to the histology of the mucosal fragments, and in 14 cases the gastric mucosa was reported as normal. Histamine test meals showed achlorhydria in 52 cases of atrophic gastritis and in 25 cases of superficial gastritis. The remainder of the cases all showed hypochlorhydria. Radiological studies usually showed a "normal" stomach.

The course of the gastritis was studied in a follow-up of the present series; the disease was found in most cases to be progressive or stationary, but rarely was there resolution of the lesion. No case of gastric carcinoma or pernicious anaemia was observed to develop from gastritis. The authors stress the impossibility of diagnosing gastritis on any other grounds than histological examination of mucosal fragments, and comment on the frequent confusion of "gastritis" with "functional dyspepsia". *I. McLean-Baird*

1160. **The Correlation between Test Meal Findings and the Histology of the Stomach as Shown by Gastric Biopsy**
J. F. FUNDER and S. WEIDEN. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 600–602, May 3, 1952. 1 fig., 6 refs.

In this communication from the Royal Melbourne Hospital the authors have attempted to show the correlation between "gastritis" and gastric function. The diagnosis of gastritis was made by gastric biopsy with the flexible gastric-biopsy tube. The histological criteria were arbitrary and depended on the percentage of parietal cells which remained in the mucosa; there were three types: (1) superficial gastritis, (2) atrophic gastritis, and (3) gastric atrophy, depending on the severity of the destruction of parietal cells.

The histamine test meal was employed and the amounts of acid and pepsin were estimated by standard methods in 268 cases. The patients in Group 1 were found to have some diminution of free acid, reduction was seen in atrophic gastritis, and all patients with gastric atrophy had achlorhydria. The secretion of pepsin was found to be diminished in a similar way, but it was noteworthy that a significant degree of pepsin secretion was found in 5 of the 12 cases of gastric atrophy associated with pernicious anaemia. The authors point out that in superficial gastritis there are abundant parietal cells, and that the finding of reduced histamine response in these cases suggests a structural change in the parietal cells not demonstrable by ordinary histological methods.

I. McLean-Baird

See also Haematology, Abstract 1219.

LIVER AND GALL-BLADDER

1161. **Atrophy of the Left Lobe of the Liver**
E. J. BENZ, A. H. BAGGENSTOSS, and E. E. WOLLAEGER. *Archives of Pathology* [*Arch. Path., Chicago*] **53**, 315–330, April, 1952. 6 figs., 28 refs.

This paper contains an analysis of the recorded information in 32 cases of severe non-cirrhotic atrophy of the left lobe of the liver encountered at the Mayo Clinic over a period of 30 years; 150 livers taken at necropsy and selected at random were used as controls. Of the 32 cases of atrophy (19 of which occurred in males and 13 in females), 12 were associated with biliary obstruction due to stone, carcinoma of the head of the pancreas, or carcinoma of the common and left hepatic ducts, in 7 cases with coincident narrowing of the lumen of the left portal vein. In 6 other cases severe malnutrition was present, and in a further 6 cases occlusion of part or all

of the portal system. In 8 cases no anatomical factors were found to account for unilateral hepatic atrophy. All the cases had been studied clinically and at necropsy.

The volume of the right lobe varied between 10 and 36 times that of the left. The most important histological findings were thickening and coarse wrinkling of the liver capsule with increase in the number of perilobar portal triads, and distortion of the lobules with variable degrees of fibrosis and absence of all but a few abortive regenerative nodules. There was extensive fibrosis in over half the cases, only irregular portions of lobules remaining. Parenchymal necrosis was noted in only 2 cases.

From these 32 cases it appears that true congenital atrophy or hypoplasia of the left lobe is extremely rare, whereas obstruction of either a branch of the portal vein or of a bile duct was present in over half the cases. The authors do not definitely conclude that the " streamlining " of the portal blood to the liver plays any part in atrophy, but they rightly emphasize that the superior mesenteric vein, carrying blood from the small intestine, flows mainly to the right lobe, while the splenic vein carries blood from the descending colon mainly to the left lobe, which thus receives less nutrient material than the right lobe. They suggest that this may be the factor at work in the cases in which there were severe malnutrition and cachexia.

[This study opens up an interesting field of thought on hepatic atrophy, and clarifies the concept of left-lobe atrophy as a clinical and anatomical entity separate and distinct from cirrhosis of the liver.] *Thomas Hunt*

1162. **Intrahepatic Obstructive Jaundice**
B. P. BILLINGTON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 663–669, May 17, 1952. 14 figs., 17 refs.

The author discusses the difficulties in diagnosis of intrahepatic biliary obstruction even when an exploratory laparotomy has been performed and the presence of carcinoma of the head of the pancreas has been excluded. A diagnosis of primary biliary cirrhosis is then suggested, but the author describes 2 cases in which carcinoma of the bile ducts within the liver was found in association with the biliary cirrhosis. Such cases are clearly very difficult, and cholangiography is suggested as a possible means of reaching the true diagnosis. *J. W. McNee*

1163. **Surgical Indications in " Silent " and Fulminant Cholecystolithiasis**
B. O. C. PRIBRAM. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **149**, 245–250, May 17, 1950. 2 figs., 7 refs.

The author carried out clinical experiments to determine the sensitivity of the biliary tract. He states that the greater part of the gall-bladder is insensitive to pain; the region near the cystic duct is sensitive; and the entrance to the cystic duct and the duct are the " trigger zone for the typical gallstone attack ", whence " not only local but remote spastic contractions may be released ". The common duct is not sensitive to touch but is sensitive to increased pressure.

He then discusses the management of patients with gall-stones but without symptoms, and of patients in whom an acute condition develops. The majority of the former, when the condition and its risks are explained, choose operation at the earliest convenient time. In patients with acute gall-bladder obstruction immediate surgery is advocated; but in patients in whom the pain is subsiding, no palpable mass is felt, and jaundice follows 12 to 24 hours after the attack, delay is the proper course. In these latter cases the serum bilirubin content must be estimated daily; if the stone remains in the common duct, operation should be performed about the eighth to tenth day.

The author discusses the relative value of cholecystectomy and cholecystostomy; he favours the former for patients with acute gall-bladder obstruction.

J. E. Richardson

See also Pathology, Abstract 1069.

PANCREAS

1164. **Pancreatico-duodenal Cancer.** (Cancer i duodenopankreas)
Y. EDLUND. *Nordisk Medicine* [*Nord. Med.*] **47**, 584–586, May 2, 1952. 14 refs.

Cancer of the pancreas is considered to account for 1 to 4% of all cancer cases, only 90 cases of carcinoma of the pancreas having been found in a series of 7,934 necropsies. Of 428 pancreatico-duodenal tumours, 368 were found in the pancreas and 60 in the duodenal papilla. The records of the Surgical Department of Falun Military Hospital from 1935 to 1949 revealed that gastro-intestinal cancer occurred approximately 25 times as often as pancreatico-duodenal cancer. Gastric cancer was observed 14 times, and carcinoma of the rectum and colon 5 times, as often. In the author's experience there is no difference in the distribution of this disease between the sexes. Emaciation, pain, and jaundice are the outstanding symptoms of pancreatico-duodenal cancer, and they appear much earlier than those of gastro-intestinal cancer, loss of weight being the first and most conspicuous symptom. Icterus is present in 90% of cases, pain in 60%. In the author's patients pain was more pronounced when the tumour was located in the body than when it was in the head of the pancreas; this may be due to infiltration into the solar plexus. Early diagnosis is of the greatest importance and, in the presence of the three cardinal symptoms, is not difficult. When jaundice is present and laboratory tests show increased phosphatase activity in the serum and a low urobilinogen content of the faeces, pointing to extrahepatic biliary obstruction, operation should be performed at the earliest date. In the absence of jaundice diagnosis may be more difficult, though radiological examination may help by revealing signs of gastric and duodenal compression and ulceration. In the duodenal juice the presence of blood and a diminished content of bile and pancreatic enzymes point to malignancy.

The author reports on 37 operations on the pancreas and 2 on the duodenal papilla carried out between the years 1932 and 1951. Most of the patients were over 60, and one-third died. In half the patients chole-

cystojejunostomy was performed, and in 3 suffering from duodenal stenosis gastro-enterostomy was carried out as well. In the remaining patients exploratory laparotomy revealed extensive carcinomatous infiltration precluding operation. Radical operation is the method of choice when the tumour is seated in the duodenal papilla, since in these cases there is less tendency towards infiltration into the lymphatics and blood vessels, and the mortality is lower than that after operations for carcinoma of the head of the pancreas. Only in 2 of 133 cases reported in the literature did the patient survive operation for more than 5 years. In carcinoma of the papilla the results were more favourable, 13 out of 64 patients still being alive 5 years after operation. The poor results of radical operation for carcinoma of the pancreas have led to the conclusion that biliary–intestinal anastomosis only should be performed, whereas the recent results in carcinoma of the papilla treated by radical operation are encouraging. Although anastomosis is not considered to be life-saving, most authors agree that this operation at least relieves the patient's symptoms.

E. S. Fountain

1165. **The Effect of Complete Vagisection and Vagal Stimulation on Pancreatic Secretion in Man**

D. A. DREILING, L. J. DRUCKERMAN, and F. HOLLANDER. *Gastroenterology* [*Gastroenterology*] **20**, 578–586, April, 1952. 2 figs., 47 refs.

Pancreatic secretion was studied in: (1) a control group of 5 young healthy patients who were convalescent from a minor operation; and (2) a group of 8 patients who had undergone oesophagogastrectomy with oesophagogastric anastomosis, an operation involving complete vagotomy. After a 12-hour fast, a double-lumen gastroduodenal tube was passed under fluoroscopic control, and gastric and duodenal secretions were collected simultaneously thereafter by continuous suction. After resting specimens had been obtained, 1·0 clinical unit of secretin per kg. body weight was injected intravenously, and secretions were collected for four 20-minute periods; a further period of collection of resting (unstimulated) secretions followed, and then 20 units of insulin was injected intravenously, secretions being collected for four 20-minute periods.

The pancreatic response stimulated by the secretin test (which is believed to act independently of vagal innervation) was statistically equivalent in the 2 groups, with values for volume, bicarbonate concentration, and amylase content corresponding to the statistical normal for this test as previously reported by one of the authors (Dreiling, *Gastroenterology*, 1950, **16**, 162), showing that the function of the pancreatic gland itself was normal in both groups. In the normal subjects vagal stimulation by means of insulin hypoglycaemia produced a pancreatic fluid of which the total volume was low and the amylase content was high as compared with the response to secretin, while the bicarbonate concentration was not increased above the resting level. In the patients in whom vagotomy had been performed, the enzyme response to insulin hypoglycaemia was notably absent, as were the responses in respect of the other two factors.

It is concluded that vagotomy does not seriously interfere with digestion in man through its effect on external pancreatic secretion, and that digestive disturbances such as diarrhoea and steatorrhoea in the post-vagotomy state are not due to pancreatic insufficiency. It is suggested that the pancreatic response to insulin hypoglycaemia may, under special circumstances, be used as a test of vagal integrity.

Joseph Parness

1166. **The Role of Alcohol in the Etiology of Pancreatitis: a Study of the Effect of Intravenous Ethyl Alcohol on the External Secretion of the Pancreas**

D. A. DREILING, A. RICHMAN, and N. F. FRADKIN. *Gastroenterology* [*Gastroenterology*] **20**, 636–646, April, 1952. 44 refs.

A review of the reports in the literature dealing with alcoholism in relation to pancreatitis revealed that the association is significant and not casual.

In the present investigation, carried out in 7 normal subjects and 5 patients with chronic pancreatitis, a double-lumen gastroduodenal tube was placed in the duodenum under fluoroscopic control. Secretin, 1·0 clinical unit per kg. body weight, was administered intravenously, and the duodenal secretion collected during four 20-minute periods. After a further 20-minute period of collection of resting (unstimulated) secretion, a 5% solution of ethyl alcohol was given intravenously, the rate of infusion being adjusted so as to obtain a state of " inebriation " within a 10-minute period; the duodenal secretion was then collected during four 20-minute periods. The dose of alcohol solution necessary to obtain the desired effect averaged 3·2 ml. per kg. body weight in the patients with chronic pancreatitis, and 2·5 ml. per kg. in the normal subjects (equivalent to approximately 8 fl. oz. (227 ml.) of whisky taken orally at one time).

In the normal subjects the pancreatic response to the secretin test in regard to volume, bicarbonate concentration, and amylase values corresponded to the statistical normal for this test. In the patients with chronic pancreatitis the pancreatic response to the secretin test was below the normal limits for volume, bicarbonate concentration, and amylase, with bicarbonate values markedly and characteristically depressed in all cases. Both the normal subjects and the patients with pancreatitis showed no pancreatic response to the intravenous infusion of alcohol in respect of volume, bicarbonate concentration, or amylase content.

It is suggested that " the role of alcohol in the production of pancreatitis is not by a direct stimulatory effect on the pancreas nor through a toxic action ", but " the oral intake of alcohol causes the pancreas (via the secretin mechanism) to secrete a large volume of pancreatic juice against an obstruction to the flow of the secretions (by spasm and edema of the papilla) ".

Joseph Parness

1167. **The Diagnosis of Chronic Pancreatitis.** (Zur Diagnose der chronischen Pankreatitis)

H. FAHRLÄNDER. *Gastroenterologia* [*Gastroenterologia, Basel*] **78**, 205–226, 1952. Bibliography.

INTESTINES

1168. **Intestinal Obstruction. Ten-year Statistical Survey at the Hospital of the University of Pennsylvania**
P. NEMIR. *Annals of Surgery* [*Ann. Surg.*] **135**, 367–375, March, 1952. 9 refs.

This report is the fourth in a series of statistical studies of intestinal obstruction as seen in cases admitted to the Hospital of the University of Pennsylvania, Philadelphia, and covers the 10-year period between 1940 and 1950.

During this time 430 cases of mechanical intestinal obstruction were treated and 358 of these cases came to operation. Certain types of case which were not considered suitable for inclusion are detailed. The cause of obstruction in the 358 cases operated upon was adhesions (129 cases), external hernia (90 cases), malignancy (84 cases), internal hernia (9 cases), volvulus (13 cases), intussusception (7 cases), stricture (13 cases), foreign body (7 cases), congenital defect (1 case), and others (5 cases). Each of these groups is discussed in detail and illustrative cases briefly described.

The operative mortality for this series was 10% compared with 11% in 1934–43, 36·3% in 1922–8, and 30·5% in 1905–22. In the second half of this series (1945–50) penicillin and the other antibiotics were freely used, but caused no appreciable reduction in the mortality. Obstruction due to malignancy, with a mortality of 20·2%, accounted for nearly half the deaths. The presence of gangrenous bowel was of serious significance in all types of case, and carried an operative mortality of 31%. In 8 of the 12 fatal cases of gangrenous bowel dark, bloody intraperitoneal fluid, similar to that produced in experimental animals subjected to strangulation obstruction, was found, and it is suggested that the outpouring of toxic intraluminal contents through a permeable intestinal wall into the peritoneal cavity and thence into the blood stream in such cases is a contributory cause of death.

A. J. Drew

1169. **Treatment of Ulcerative Colitis with Corticotrophin (ACTH) and Cortisone**
S. J. GRAY, R. W. REIFENSTEIN, J. A. BENSON, and J. C. G. YOUNG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1489–1497, April 26, 1952. 4 figs., 9 refs.

The authors report from Boston some favourable results of treatment with corticotrophin and cortisone in 8 cases of ulcerative colitis which had proved intractable to prolonged and extensive medical treatment. Patients were maintained on a moderately unrestricted bland diet, and all other medication, except for the use of phenobarbitone, was discontinued. Some patients receiving corticotrophin were given penicillin injections during withdrawal of the drug. Salt and fluid intake were restricted and potassium intake was augmented. Psychological factors were excluded by the use of placebos. Treatment was controlled by a large range of laboratory tests. The rationale for this form of treatment, together with the complications of the treatment and its withdrawal, is discussed. Criteria for remission were: control of diarrhoea, decrease in faecal blood, fall in lysozyme titre (which is claimed to parallel the course of the disease), disappearance of fever, decrease in erythrocyte sedimentation rate, increase in body weight, and sigmoidoscopic evidence of healing.

The initial symptomatic response was considered excellent in 3, good in 2, and fair in 2; in the other case there was no response. None of the patients was cured, and no signs of healing were observed on sigmoidoscopic examination until after 3 weeks of treatment, when there were less bleeding and ulceration and diminished granularity. In one case with multiple strictures, polyposis, and fistulae there was no improvement and bleeding continued. A normal radiographic appearance was never achieved, though there was improvement in 3 cases.

Treatment varied in regard to both size of dose and duration, but the best long-term results were obtained after a prolonged course. Of the 7 cases which responded to treatment, remission lasting from 10 to 28 months was obtained in 4, but in the others relapse occurred from 2 to 9 months after stopping treatment. The treatment was found useful as a preparation for surgery [though the authors do not discuss this aspect further].

The dose of corticotrophin was 20 to 40 mg. intramuscularly every 6 hours for 3 to 8 weeks, with gradual reduction of dosage over the last 5 to 7 days. Later it was given intravenously, 20 mg. in 500 ml. of dextrose over an 8-hour period daily. Cortisone was given orally in one or more courses of 100 to 125 mg. twice daily for 10 to 21 days, again with gradual reduction in dosage. The longest course of treatment was 133 days.

J. David DeJong

1170. **Anal Abscess and Anal Fistula: Results of Treatment.** (Analabscesser og analfistler. Behandlingsresultater)
O. POULSEN. *Nordisk Medicin* [*Nord. Med.*] **47**, 447–450, April 4, 1952. 1 fig., 5 refs.

The author presents a survey of all perianal abscesses and anal fistulae treated during 13 years in a surgical unit of the Bispebjerg Hospital, Copenhagen; 142 out of 211 patients with abscess and 82 of 96 with fistula were followed up. *Bacterium coli*, staphylococci, and streptococci were isolated from the great majority of abscesses, singly or in mixed culture. Treatment of the abscesses consisted in simple incision, but the high rate of recurrence (23·2%) suggested to the author the desirability of radical operation. Of the fistulae 40% were divided and 60% excised; 34 patients had to undergo more than one operation, and 4 of these, all with extra-sphincteric fistulae, suffered from incontinence in spite of suture of the sphincter. On the basis of his survey the author recommends treatment of fistulae by wide excision with vertical division of the sphincter and without muscle suture.

W. G. Harding

1171. **Cancer of the Rectum Diagnosed by Sponge Biopsy**
S. A. GLADSTONE. *American Journal of Surgery* [*Amer. J. Surg.*] **83**, 664–670, May, 1952. 4 figs., 7 refs.

Cardiovascular System

1172. **Acute Non-specific Pericarditis.** (Les péricardites aiguës non spécifiques)
Y. Bouvrain and F. Costeas. *Presse Médicale* [*Pr. méd.*] **60**, 781–782, May 24, 1952. 19 refs.

The authors report 2 cases of acute non-specific pericarditis in which the predominating symptom was precordial pain. Both patients were female, aged 42 and 62 respectively. The pain was made worse by deep breathing. In addition to a pericardial effusion the patients had a pleural effusion, which in both cases was identical in cytology and mainly lymphocytic. In these 2 cases the pericarditis followed mild upper respiratory infections, and subsided in 3 to 4 weeks without any apparent permanent damage to the heart, although in one case the pain persisted for several months.

The aetiology of the condition is unknown. There was no increase in the cold agglutinins, and the antistreptolysin titre remained normal. The authors suggest that aureomycin should be tried in the treatment. Culture of the pericardial fluid on Loewenstein's medium was negative, but the possibility of a tuberculous aetiology cannot be entirely ruled out. Similar cases reported in the literature are discussed. *G. S. Crockett*

1173. **Chronic Cardiac Aneurysm.** (Das chronische Herzaneurysma)
B. Steinman and M. Elsaesser. *Helvetica Medica Acta* [*Helv. med. Acta*] **19**, 42–65, March, 1952. 4 figs., bibliography.

This article is based on personal observation of 31 cases of aneurysm of the heart and includes a good review of the literature. The authors suggest that the condition is not so rare as is generally supposed and that its clinical, radiological, and cardiographic signs should be more carefully looked for. A persistently raised S–T segment in the chest leads taken over the left ventricle (the most frequent site of aneurysm) is very suggestive of its presence. *G. S. Crockett*

1174. **Antibiotic Therapy of Bacterial Endocarditis.—I. Experiences with Terramycin in the Treatment of Subacute Bacterial Endocarditis**
J. E. Geraci. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **27**, 169–180, April 23, 1952. 36 refs.

Terramycin was given to 9 patients with subacute bacterial endocarditis, in whom the infecting organism was sensitive *in vitro* to terramycin. In 3 of the cases terramycin alone was ineffective; in the remaining 6 a combination of terramycin and streptomycin resulted in cure in one case only, in spite of an apparently satisfactory immediate response to the antibiotics.

The author's investigations suggest that terramycin has a very limited application in the treatment of subacute bacterial endocarditis. The antibiotic is, however, of value when an organism is isolated that is sensitive to terramycin but resistant to penicillin, or where there is an allergic response to the use of penicillin. It is more effective when combined with streptomycin, and is then particularly suitable for the treatment of streptomycin-sensitive Gram-negative organisms. Anorexia, nausea, vomiting, and occasionally diarrhoea are the chief, and not uncommon, indications of toxicity.

James W. Brown

1175. **Failure of Ligation of the Left Auricular Appendage in the Prevention of Recurrent Embolism**
F. C. Leonard, and M. A. Cogan. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 733–735, May 8, 1952. 11 refs.

The authors point out that once a patient has had an embolism in an attack of rheumatic heart disease he may have a recurrence of the embolism at any time. The majority of emboli are thought to originate from the left auricular appendix, and therefore this structure has been amputated in the hope of preventing a clot from forming and spreading. It would appear, however, that this procedure is not adequate as a clot may well form within the cavity of the auricle proper.

The administration of dicoumarol and of anticoagulants over a prolonged period has proved to be the best treatment so far, and the authors consider that unless clots within the heart can be localized resection of the auricular appendix should be abandoned.

T. Holmes Sellors

1176. **Studies of Plasma Quinidine Content.—III. The Value of Delayed Absorptive Coated Tablets in Oral Quinidine Therapy**
J. J. Sampson, H. Foreman, and B. C. Solomon. *Circulation* [*Circulation*] **5**, 534–538, April, 1952. 3 figs., 7 refs.

Gastro-intestinal upset usually occurs in quinidine therapy when the blood level of the drug exceeds 5 mg. per litre, but in certain individuals signs of intolerance develop at much lower levels. If this is due to a hypersensitivity of the stomach and upper intestine, the use of coated tablets might prevent it by delaying absorption, and might also be useful in obviating the waking of a patient at night to give a dose of quinidine. There is evidence that absorption from the large bowel is satisfactory and that therapeutic blood levels may be obtained by rectal administration.

In experiments which were carried out at Mount Zion Hospital, San Francisco, 7 subjects were given 0·6 to 0·8 g. of quinidine in enteric-coated tablets; the maximum blood quinidine level occurred 5 to 12 hours after administration, and the level was still 66% of the peak value after 12 hours. Of 10 patients with cardiac arrhythmia who had shown signs of gastro-intestinal

sensitivity to quinidine, 7 tolerated the enteric-coated tablets well, though 6 had some bowel upset—probably at higher blood levels than formerly. Of these patients 6 were relieved of their arrhythmia. It is important to note that inadequate absorption may occur if the tablets are used after prolonged storage. *A. Paton*

CARDIOGRAPHY

1177. **The Electrocardiogram in Pregnancy.** (L'électrocardiogramme de la femme enceinte)
J. MONIZ DE BETTENCOURT and J. C. BARRETO FRAGOSO. *Acta Cardiologica* [*Acta cardiol., Brux.*] **7**, 123–139, 1952. 9 figs.

At St. Joseph's Hospital, Lisbon, the authors recorded 12-lead electrocardiograms from 115 normal pregnant women, from 37 of whom tracings were taken both before and after delivery. In the majority, as pregnancy advanced the heart became more horizontal and the QRS axis deviated to the left. As there was reversion to the original position after delivery, this change was attributed to elevation of the diaphragm during pregnancy. In only 2 cases was there electrocardiographic evidence of left ventricular hypertrophy developing during pregnancy and disappearing after delivery. In a few cases pregnancy appeared to cause right axis deviation; the suggestion is made that this may have been due not to any change in position, but to the presence of the distended uterus causing better conduction of the cardiac electrical potential changes to the leg lead. [However, no evidence is given that these few patients differed from the remainder in the size or position of the uterus.]
J. A. Cosh

1178. **The Electrocardiographic Diagnosis of Acute Cor Pulmonale**
M. ELIASER and F. GIANSIRACUSA. *American Heart Journal* [*Amer. Heart J.*] **43**, 533–545, April, 1952. 7 figs., 16 refs.

The electrocardiographic changes seen in 8 cases of massive pulmonary embolism at the San Francisco Hospital (University of California Service) are presented and discussed. Clockwise rotation of the heart, with consequent displacement of the transition point in the chest leads towards the left, is stated to have been observed in all 8 [though not apparent in all the illustrations]. The heart usually became more vertical in position. Inversion of the T wave in right-sided chest leads was seen in 4 cases, and is attributed to right ventricular strain. Depression of the S–T segment or inversion of T (or both) was seen in the left-sided chest leads in 4 cases, and is attributed to myocardial ischaemia. Auricular fibrillation was clearly precipitated by the embolism in one case, and transient right bundle-branch block in another.

[In some of the case descriptions there is ambiguity as to the precise date of the pulmonary embolism and as to the nature of pre-existing heart disease and of any initial electrocardiographic changes due to such disease.]
J. A. Cosh

CONGENITAL HEART DISEASE

1179. **The Pulmonary and Systemic Circulation in Congenital Heart Disease**
D. C. DEUCHAR and R. KNEBEL. *British Heart Journal* [*Brit. Heart J.*] **14**, 225–249, April, 1952. 9 figs., 43 refs.

The haemodynamic findings in a series of 24 patients with congenital heart disease at Guy's Hospital, London, have been critically analysed. Cardiac output and peripheral resistance were calculated in the usual manner, and in addition the formulae of Broemser and Ranke have been applied to calculate the part played by changes in the elasticity of the pulmonary artery in the production of changes in pulmonary pressure.

In atrial septal defect the peripheral resistance in the lungs is low and the elasticity resistance of the pulmonary arteries is also low, so that the pulse pressure is not increased in the pulmonary arterial system despite the high stroke volume in such patients. In ventricular septal defect an increased systolic and pulse pressure in the pulmonary vessels is entirely accounted for by an increased stroke output, but in some instances there is an increased peripheral resistance in the pulmonary arterioles as well. In cases with Eisenmenger's complex the pulmonary peripheral resistance and elasticity resistance are both grossly increased. In pulmonary stenosis the right ventricular pressures are high and the pulmonary arterial pressures, while usually low, may in some instances be above the normal. With a reduced minute output of the heart, the raised pulmonary arterial pressures may indicate a very high peripheral vascular resistance in the lungs. Where the pulmonary arteries are large the elasticity resistance of their walls is small, as might be expected; and when the pulmonary arteries are small the elasticity resistance of their walls is high: in short, elastic recoil is greater with capacious main arteries than with small main arteries. Brief cardiological histories of the 24 cases are given.
J. McMichael

1180. **Atresia of the Tricuspid Orifice.** (Die Tricuspidalatresie)
A. SCHAEDE. *Deutsches Archiv für klinische Medizin* [*Dtsch. Arch. klin. Med.*] **199**, 102–120, 1952. 19 figs., 43 refs.

At the Medical Clinic, Bonn, 12 cases of tricuspid atresia were observed; in 2 of the cases the diagnosis was confirmed at necropsy. In these cases the circulation is maintained via an open interauricular septum, and the pulmonary supply is conducted either through a patent interventricular septum to the right ventricle or, in cases of atrophy of the right chamber, via a patent ductus arteriosus. The condition occurs with or without transposition of the large vessels; the mechanics of the circulation are more favourable when there is transposition. A straight right border of the heart radiologically and electrocardiographic signs of left ventricular hypertrophy, together with cyanosis and clubbing, are suggestive features. Angiocardiography shows characteristic transit of the contrast medium from the right to the left

auricle. The inadequate filling of the pulmonary circulation, which is evident in most cases, forms the indication for Blalock's operation. *G. Schoenewald*

1181. **Tricuspid Atresia Associated with Transposition of the Heart.** (Inversion des Herzens und Tricuspidalatresie)
A. SCHAEDE. *Deutsches Archiv für klinische Medizin* [*Dtsch. Arch. klin. Med.*] **199**, 121–129, 1952. 9 figs., 7 refs.

The author describes two cases of dextrocardia with tricuspid atresia. The first case, of which details obtained at necropsy are given, was also of interest in that although there was almost complete absence of the interventricular septum, the electrocardiogram yet showed normal RS complexes. The author feels that this argues against the function of the bundle of His as a specific conduction system, though he has not excluded an abnormal course of the bundle in this case.
G. Schoenewald

1182. **Congenital Malformations of the Heart Associated with Dextrocardia.** (Contribution à l'étude des malformations cardiaques congénitales associées aux dextrocardies)
P. SOULIÉ, J. DI MATTÉO, A. PITON, and A. SIBILLE. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 1334–1344, April 30, 1952. 18 figs., 30 refs.

With the growth of cardiac surgery the problem of congenital abnormalities of the heart has become of increasing practical importance. The authors of this paper divide dextrocardia anatomically into two main groups: (1) dextrocardia with inversion of the cavities (situs inversus cordis), which is often associated with total inversion of the viscera (situs inversus totalis) and of which situs inversus with secondary laevocardia is another form; (2) dextrocardia without inversion of the cavities, called also situs sagittalis. The recognition of conditions of abnormal orientation of the ventricles is most important in chest surgery. Of the 24 cases of abnormal orientation in the authors' series, 16 were associated with some other abnormality of the heart.

These conditions of abnormal orientation are often missed by routine clinical, radiological, and electrocardiographic examination. Angiocardiography and cardiac catheterization are necessary for their proper investigation. Five cases are reported in detail with the results of the investigations, and the diagnosis is discussed. *Peter Harvey*

CORONARY THROMBOSIS

1183. **Prolonged Anticoagulant Therapy with Heparin**
A. WYNN, J. F. GOODWIN, and A. BIRBECK. *British Medical Journal* [*Brit. med. J.*] **1**, 893–896, April 26, 1952.

Administration of anticoagulants is now firmly established as good practice in the treatment of coronary thrombosis and other forms of intravascular clotting, but it is not a safe procedure over a long period without adequate knowledge of blood chemistry in relation to clotting. The authors give heparin, intravenously at first then intramuscularly, and estimate the coagulation time, not the prothrombin time; the coagulation time can be estimated once a day without much difficulty.

In clinical practice 50 mg. of heparin is given intravenously by slow drip into a wrist vein every 4 hours for 10 days, the coagulation time being safely raised from 6 minutes to twice or three times that figure. Ten days is the limit for intravenous therapy; thereafter the anticoagulant must be given by intramuscular injection. A useful standard procedure, which will, of course, need modification according to the coagulation time, is to give 150 mg. of heparin in isotonic solution with 2 ml. of 1% procaine. The injection must be slow and gentle, with pressure upon the site immediately on withdrawal of the needle; it should be given every 12 hours for 10 to 14 days.

This procedure is not suitable in elderly people with lax subcutaneous tissue or in those who tend to bruise easily. *G. F. Walker*

1184. **The Adrenal Function in Coronary Thrombosis.** [In English]
O. FORSSMAN, G. HANSSON, and C. C. JENSEN. *Acta Medica Scandinavica* [*Acta med. scand.*] **142**, 441–449, April 30, 1952. 2 figs., 27 refs.

The authors investigated adrenocortical and adrenomedullary function in coronary thrombosis, to determine whether the stress of the disease caused an increase in the function of the gland. In 14 out of 15 cases there was a marked rise in the urinary excretion of catechol, suggesting an increase in secretion of adrenaline and noradrenaline. Urinary excretion of 11-oxysteroids and 17-ketosteroids was raised in about half the cases. Eosinopenia was found in most severe cases, but the number of circulating eosinophils returned to normal within 8 days. *G. S. Crockett*

1185. **"Armchair" Treatment of Acute Coronary Thrombosis**
S. A. LEVINE and B. LOWN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1365–1369, April 19, 1952. 2 figs., 12 refs.

In 81 cases of acute coronary thrombosis treated at home and at the Peter Bent Brigham Hospital, Boston, the patients were encouraged at the end of the first week of their illness to spend the greater part of each day sitting in a comfortable chair with their legs dependent; shock, marked debility, or cerebral vascular accidents were the only contraindications. The authors hold the view that this method reduces cardiac output, discourages pulmonary congestion, and reduces the incidence of thrombophlebitis and other complications. All the other methods of treatment usually employed in coronary thrombosis were also used.

In this uncontrolled series, in which there were 8 deaths (9·9%), the results were held to be satisfactory, and the method appeared especially valuable in patients with congestive heart failure. The beneficial psychological effect of the manœuvre in reducing feelings of anxiety is also stressed. *J. W. Litchfield*

1186. **Anoxia in Myocardial Infarction and Indications for Oxygen Therapy**

C. W. BORDEN, R. V. EBERT, and R. H. WILSON. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1370–1371, April 19, 1952. 1 fig., 14 refs.

At the Veterans Administration Hospital, Minneapolis, oxygen saturation of the arterial blood was measured in 23 patients with recent myocardial infarction. In those patients without pulmonary oedema (diagnosed on clinical or radiological grounds) or shock, the mean value was 94·1%, and in those with these complications it was 80·8%. The authors conclude that oxygen therapy is essential only in those patients with pulmonary oedema or shock, and if used in other cases should be given in high concentration by B.L.B. mask to give a maximum amount of oxygen in physical solution. [It is assumed, but not proved, that a satisfactory rise in oxygen saturation can be obtained.] *J. W. Litchfield*

1187. **Indications for Bishydroxycoumarin (Dicumarol) in Acute Myocardial Infarction**

H. I. RUSSEK, B. L. ZOHMAN, A. A. DOERNER, A. S. RUSSEK, and L. G. WHITE. *Circulation* [*Circulation*] **5**, 707–711, May, 1952. 11 refs.

A series of 623 patients suffering from myocardial infarction was divided into two groups according to the history and the facts elicited at a physical examination carried out during the first 24 hours in hospital. In the first group were 338 " poor risk " patients in whom one or more of the following were noted: evidence of previous myocardial infarction; intractable pain; extreme degree or persistence of shock; marked cardiac enlargement; gallop rhythm; congestive heart failure; auricular fibrillation or flutter, ventricular tachycardia or intraventricular block; diabetic acidosis; marked obesity; varicose veins; or evidence of previous thromboembolism. In the second group were 285 patients in whom none of these signs and symptoms was noted, these being classified as " good risk " patients. All the patients were treated conservatively. In the first group the mortality in hospital was 70% and the incidence of thrombo-embolism was 12·4%, compared with 3·5% and 0·7% respectively in the second group.

The authors suggest that it is pointless to subject patients in the " good risk " category to the hazards of anticoagulant therapy for the sake [as they calculate] of a theoretically preventable mortality of about 1%.

R. S. Stevens

1188. **Evaluation of Dicumarol Therapy in 287 Cases of Acute Myocardial Infarction**

I. A. RASHKOFF, L. E. SCHAEFER, M. G. MAGIDA, and H. LEVY. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **18**, 350–357, March–April, 1952. 18 refs.

Of 287 patients with uncomplicated myocardial infarction who survived the first day in hospital, 142 received dicoumarol and 145 served as controls; except for the administration of dicoumarol both groups were treated in the same way. As regards age and sex of the patients, history of previous myocardial infarction, severity of the illness before admission, and frequency of administration of digitalis, there was no statistically significant difference at the 5% level of probability between the two groups. The dose of dicoumarol was 300 mg. on the first day and 200 mg. on the second; subsequently the dose was adjusted to maintain the prothrombin time at a level between 2 and 2½ times the control time. The drug was given until the patients became ambulant (average 5 weeks).

The death rate in the group receiving dicoumarol was 13%, and in the control group 27%. The incidence of thrombo-embolic complications was 14% in the former group and 26% in the controls. Death in the series was associated with clinically evident thrombo-embolic phenomena in 4% of the dicoumarol-treated cases and 10% of the control group. Minor haemorrhagic complications were encountered in 8 cases. In one further case death may have been due to dicoumarol; the patient died suddenly of heart failure and on the day of death the prothrombin time was 76 seconds (control time 12 seconds). It is concluded " that acute myocardial infarction should be treated with anticoagulants routinely except when recognized contraindications are present ".

A. Schott

1189. **L-Arterenol (Levophed) in the Treatment of Shock due to Acute Myocardial Infarction**

A. J. MILLER and L. A. BAKER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 591–599, April, 1952. 15 refs.

The authors have experimented with " L-arterenol " (noradrenaline) in the treatment of the hypotensive state, " cardiogenic shock ", that may accompany acute myocardial infarction. They argue that the fall in left ventricular output resulting from the infarction reduces the aortic pressure and coronary blood flow with consequent ischaemia of the non-infarcted myocardium. The purpose of giving pressor drugs is to restore the blood pressure to normal and to ensure adequate coronary blood flow. This should militate against extension of the infarct and help to restore an adequate cardiac output. Indications for use were a clinical diagnosis of recent acute myocardial infarction and a systolic blood pressure of 80 mm. Hg or less for at least 4 hours. The noradrenaline was given in a solution containing 1·0 mg. per litre of 5% glucose or 0·9% sodium chloride in water intravenously at a maximum rate of 60 drops a minute.

In 4 of 7 patients given injections of noradrenaline there was a significant rise in the blood pressure. One of the 4 was the sole survivor; in the other 3 patients peripheral vascular failure and death occurred soon after the noradrenaline had been discontinued. Three patients failed to respond adequately to noradrenaline; one of these also had gastro-intestinal haemorrhage and the other 2 were very near death when treatment was started. No adverse effects or change in prevailing cardiac rhythm were noted during administration of the drug.

The authors conclude that a further trial of this drug in the treatment of cardiogenic shock is warranted, possibly in combination with intra-arterial transfusion.

K. G. Lowe

1190. **Acute Cardiac Infarction without Pain**
C. PAPP. *British Heart Journal* [*Brit. Heart J.*] **14**, 250–260, April, 1952. 9 figs., 17 refs.

In a series of 150 cases of cardiac infarction seen at Charing Cross Hospital, London, 7 patients (4·7%) had no pain at all. In 3 of these congestive heart failure was present before the relevant infarction occurred; in all 3 acute paroxysmal dyspnoea was the main symptom. In the remainder complete heart block had developed, and although the patients were aware of faintness with bradycardia, there was no classical Stokes–Adams attack. The prognosis in these two groups is considered to be serious. *J. McMichael*

HEART FAILURE

1191. **Clinical Use of Cation Exchange Resins in the Treatment of Congestive Heart Failure**
E. J. CALLAHAN, N. R. FRANK, H. KRAUS, and L. B. ELLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 117–125, Feb., 1952. 20 refs.

The authors reaffirm the value of a cation-exchange resin (an ammonium–potassium-cycle carboxylic resin) in the treatment of congestive cardiac failure. Patients receiving the resin were able to eat a more liberal diet, particularly as regards sodium, which was made unabsorbable by the resin. Mercurial diuretics could be reduced while the patients were taking the resin.

All toxic effects were manifested clinically, and the authors consider that elaborate laboratory studies are not necessary in following the progress of the treatment. Gastro-intestinal symptoms such as nausea, anorexia, vomiting, and constipation were the commonest complications of treatment. Digitalis intoxication also occurred fairly often, but the reason for this remains obscure. The commonest electrolyte disturbances were those of hypocalcaemia and hypokalaemia, with a compensated acidosis. *G. S. Crockett*

1192. **Use of a Combination of Anion and Cation Exchange Resins in the Treatment of Edema and Ascites**
B. L. MARTZ, K. G. KOHLSTAEDT, and O. M. HELMER. *Circulation* [*Circulation*] **5**, 524–533, April, 1952. 4 figs., 21 refs.

Cation-exchange resins take up sodium and potassium in return for ammonium ions, and their administration in the treatment of oedema tends to cause acidaemia; it may also cause excessive potassium depletion, but this can be prevented by using equal parts of the potassium and ammonium resins. The administration of large doses of the potassium resin, however, may lead to hyperkalaemia owing to inability of the kidney to excrete the excess potassium, and this is especially so if oliguria is present. A mixture of one-third potassium and two-thirds hydrogen resins was therefore used by the authors in treating 12 patients with congestive heart failure for 2 to 13 months, but again acidosis tended to occur, especially in those with damaged kidneys.

To overcome these difficulties a mixture was finally evolved which contained 12% of a weakly basic anion-exchange resin and 88% of mixed cation-exchange resins (29% potassium and 59% hydrogen resin). The carboxylic rather than the sulphonic type of cation-exchange resin was chosen because of its greater activity, and a resin in the hydrogen rather than the ammonium cycle because of its greater palatability. The addition of the anion-exchange resin not only prevented acidosis, but also increased the uptake of sodium by the cation-exchange resins; the latter effect was greatest in those patients receiving the lowest quantity of sodium in the diet. The effect of mercurial diuretics was potentiated. No effect on calcium, phosphorus, or iron metabolism was noted. A total quantity of 30 to 60 g. of the resin mixture a day in divided doses proved very satisfactory in the treatment of 42 patients with congestive cardiac failure and 14 with cirrhosis of the liver, who were maintained on a 1·5-g. sodium diet and were treated continuously for periods of not less than 4 months, only 4 of these patients being unable to tolerate the dose because of gastro-intestinal symptoms and 2 others because of an exacerbation of pre-existing anginal symptoms. Of the remaining 50 patients a few showed changes in bowel action, but no serious electrolyte disturbances were observed. *A. Paton*

AORTA

1193. **On Occlusion of the Abdominal Aorta**
C. C. BURT, J. LEARMONTH, and R. L. RICHARDS. *Edinburgh Medical Journal* [*Edinb. med. J.*] **59**, 65–93 and 113–142, Feb. and March, 1952. 37 figs., bibliography.

The authors have divided their exhaustive review of the subject of occlusion of the abdominal aorta into three parts, of which the first is introductory, the second deals with aortic thrombosis, and the third with aortic embolism. The introduction covers the historical aspects, and includes a discussion of the anatomical, physiological, and pathological factors involved. Congenital anomalies of the aorta, even when associated with narrowing, rarely lead to blocking, but one such anomaly in which the external iliac artery on one side originates direct from the aorta may be of clinical importance. In such a case the bifurcation, consisting of one common iliac artery and one internal iliac artery, may be obstructed and yet the circulation to one limb be preserved. The cause of occlusion is thrombosis or embolism or a combination of both. Thrombosis is usually due to disease of the vessel wall (rarely syphilitic), but is occasionally secondary to an aneurysm; pressure from without has also been reported as a cause. The collateral circulation which develops in response to occlusion of the aorta is discussed, the possible importance of visceral channels being mentioned. When the aorta is occluded at its termination, blood reaches the legs through the communications between the terminal branches of the inferior mesenteric artery and branches of the internal pudendal, superior and inferior gluteal, obturator, and circumflex arteries, and by somatic channels. This collateral circulation may be sufficient

to maintain the blood supply to the legs if the occlusion develops slowly.

Details are given in the second part of 11 cases in which aortic thrombosis was diagnosed. The patients' ages ranged from 35 to 57 years. The onset was gradual in 10 patients and sudden in one, in whom there was no evident source of embolism. In one patient aortic occlusion followed two separate embolic episodes in the legs, the thrombosis having apparently extended in a retrograde fashion up each leg to occlude the bifurcation of the aorta. The symptoms consisted of intermittent claudication (with pain in the buttocks in 2 cases) and coldness of the feet. Four patients noted weakness, and 4 swelling, of the legs. On examination, absence of pulses in the lower limbs was the most constant feature, while the femoral pulses were absent in 8 cases and abnormal in the remainder. Other signs of vascular insufficiency were present in addition, but the skin nutrition was good in 8 cases, only 3 patients showing gangrenous or pre-gangrenous lesions. Neurological abnormalities of varying severity were present in most cases. Special investigations consisted in oscillometry, measurement of calf blood flow before and after exercise, and aortography. Plethysmography showed a delayed increase in flow after exercise and delayed return to the resting level, as in occlusive vascular disease. Aortography was on the whole unsuccessful. The prognosis for life and preservation of limbs may be surprisingly good, although claudication is severe. In the early stages high bilateral sympathectomy may improve the collateral circulation if the aorta and iliac arteries are not extensively diseased, but is not without risk in advanced cases. The authors have no personal experience of resection of the aortic bifurcation.

In the third part 16 cases of embolic occlusion of the terminal aorta are described and analysed, auricular fibrillation due to rheumatic heart disease being the cause in the majority. The onset was sudden in all but 2 cases, and pain was usually the initial symptom. The clinical course may be divided into 3 stages: (1) up to 6 hours; (2) 6 to 48 hours; and (3) 48 to 72 hours after the incident. During Stage 1 partial paralysis of the limbs may develop; in Stage 2 muscle contractures develop and sensory and motor loss becomes complete; and in Stage 3 the muscles soften and the limbs swell. The prognosis is good in Stage 1, but becomes progressively worse until, in Stage 3, amputation is inevitable. The authors discuss the clinical features in detail with special reference to the neurological manifestations, and make recommendations for treatment. They consider that ischaemia of the lumbo-sacral plexus and peripheral nerves is the principal cause of the motor and sensory paralysis, and that the rapidity of onset of motor and sensory loss and their extent depend upon the completeness of the obstruction and the distribution of any reflex vasospasm. When the diagnosis is suspected heparin should be injected intravenously, morphine given for pain, and the trunk and arms should be heated to produce reflex vasodilatation. If no improvement is observed, embolectomy should be performed after the heparin has been neutralized with protamine sulphate.

[It is impossible to do full justice to this excellent and comprehensive paper in an abstract. Those interested are advised to consult the original work.]

J. F. Goodwin

ARTERIES

1194. **The Treatment of Aneurysms with Fibroblastic Agents. Experimental and Clinical Studies with the Use of Sodium Dicetyl Phosphate**

J. K. BERMAN and J. E. HULL. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **94**, 543–549, May, 1952. 6 figs., 4 refs.

It was found from animal experiments that dicetyl phosphate (the chemistry of which is described), when injected into the adventitia of large arteries, produced a marked perivascular fibrositis with great thickening of the arterial wall. It seemed, therefore, that injections of dicetyl phosphate into the outer layers of an aneurysm might lead to thickening and increased resistance of the wall. The method was tried in 5 patients with aortic aneurysm, and in those in whom there was no evidence of dissection the results appeared to be favourable.

[It is considerably less risky to inject 75 to 100 ml. of solution around an aneurysm than to dissect out an aneurysm and wrap it in "cellophane". It may be that a combination of cellophane wrapping and perianeurysmal injection will give the best results, the latter procedure being restricted to the area where dissection is most difficult.] *Peter Martin*

1195. **Intra-arterial Histamine in the Treatment of Occlusive Peripheral Arterial Disease**

J. A. DIXON, W. J. M. SCOTT, and M. A. EPSTEIN. *Circulation* [*Circulation*] **5**, 661–669, May, 1952. 7 figs., 19 refs.

From the University of Rochester, New York, comes this report of the treatment of 7 male patients (average age 64 years) suffering from intermittent claudication by repeated intra-arterial infusion of histamine. They were given 3 mg. of histamine diphosphate in 500 ml. of normal saline infused into the femoral artery over a period of half an hour. The usual course of treatment was two injections per week for the first 3 weeks, then one injection per week until the maximum increase in exercise tolerance had been reached. The patients studied were thought to have ischaemia mainly as a result of arterial occlusion rather than of spasm, because of their poor response to reflex heating, posterior tibial nerve block, and paravertebral block.

The immediate effect of the injections was an erythema of the skin corresponding roughly to the distribution of the unobstructed vessels, followed by "goose-flesh" and scattered areas of weal formation. The thigh skin temperature rose early, and there was a marked increase on standing. The effects of the injections on the general circulation were studied by ballistocardiography, femoral arterial and venous pressures being recorded, and blood samples were obtained from the femoral artery and vein. In most subjects there was an increase in heart rate,

stroke volume, cardiac output, and oxygen saturation in the femoral vein. The femoral arterial blood pressure, oxygen saturation, and arteriovenous oxygen difference decreased. These changes did not occur when intra-arterial normal saline was given.

The results of treatment were judged by the response to a standard walking test on a treadmill. Five patients achieved an early and marked increase in exercise tolerance and were assessed as having a good result, one patient had a fair result, and one no improvement. Improvement generally began after 6 injections had been given. The authors conclude that the effects of intra-arterial histamine resemble those seen in arteriovenous shunts, and that the beneficial results might be due to acute arteriovenous shunting with consequent improvement in the collateral circulation. *J. F. Goodwin*

1196. **Endarteriectomy, or Surgical Restoration of the Lumen of an Obstructed Artery in Arteriosclerosis Obliterans. A Preliminary Report**
A. N. NÚÑEZ, B. MILANÉS, and J. R. INIGO. *Circulation* [*Circulation*] **5**, 670–679, May, 1952. 10 figs., 18 refs.

The authors, who write from the University Hospital, Havana, Cuba, define endarteriectomy as the restoration of the lumen of an obstructed artery by excision of the fixed thrombus together with the intima to which it is attached. The earlier work of Dos Santos, Leriche, and others is quoted. The anatomical basis for the operation is the existence of a plane of cleavage between the endothelium and media of the artery. After endarteriectomy the lumen has a rough lining which favours thrombosis, but this can be prevented by anticoagulant therapy, which is essential for success. In selecting cases it is important to study the arterial tree by means of arteriography, the ideal indication being an occlusion of limited extent in a large vessel, with a patent segment distal to the block. However, even when thrombosis involves a long segment some improvement in blood flow may occur. The most favourable results may be expected in soft elastic arteries rather than in those with hardened calcareous walls. The operation was performed on 4 patients, with satisfactory results in 3, but the fourth patient died from pulmonary embolism and retroperitoneal haemorrhage.

[Details and diagrams of operative technique are given, and readers interested in these practical points are advised to consult the original article.]

J. F. Goodwin

1197. **Intraarterial Priscoline Therapy for Peripheral Vascular Disturbances**
H. I. LIPPMANN. *Angiology* [*Angiology*] **3**, 69–97, April, 1952. 6 figs., 9 refs.

"Priscol" (tolazoline) was given by intra-arterial injection to 80 patients with peripheral vascular disease, the object being to achieve a sustained vasodilatation which could be maintained with regular injections. The amount of priscol administered was determined by the "maximum local dose" which did not produce any systemic reactions. The initial dose was 20 mg. in the leg and 12·5 mg. in the arm. If a general reaction occurred (increase in pulse rate, fall in blood pressure, flushing in other limbs) subsequent doses were decreased by 2·5 mg. until the maximum local dose was determined. This dose was then given in all subsequent injections. The local reactions were flushing of the limb, with a burning sensation and often "goose-flesh", and an increase in skin temperature and oscillometric and plethysmographic readings. The majority of patients received 2 or 3 injections a day for 3 to 10 days, 1 or 2 daily for 7 days, and then 1 daily until continuous vasodilatation was achieved. No significant side-reactions were noted if the maximum local dose was adhered to. Contraindications were repeated systemic reactions after an injection of less than 10 mg. (these were observed in 15% of patients); decrease in flow following injection; and oedema of the area surrounding gangrenous lesions.

Of 11 patients with gangrene of the heel 8 were cured, amputation being required in 3; in a control group of 11, 9 required amputation. Of 49 patients with ischaemic lesions in other parts of the limbs as a result of occlusive vascular disease, 26 required amputation, healing occurring in 23; most of these patients were elderly and in poor condition. In 4 cases of advanced gangrene intra-arterial injection of priscol was thought to permit more conservative amputation. The drug was given in 7 cases of acute arterial occlusion (2 of embolism); both patients with embolism recovered without trophic lesions, but 2 of the 5 with thrombotic occlusion required amputation. In 4 cases of iliofemoral thrombophlebitis there was evidence of arterial insufficiency in the same limb, which was attributed to spasm of the artery; symptoms rapidly resolved with treatment. The results in Raynaud's disease were not striking. There was further increase in blood flow to the skin after intra-arterial injection of priscol in patients who had undergone sympathectomy. *J. F. Goodwin*

1198. **The Treatment of Intermittent Claudication**
M. HAMILTON and G. M. WILSON. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **21**, 169–183, April, 1952. 3 figs., 33 refs.

A critical evaluation of the effect of the current remedies for intermittent claudication has been made in a series of 40 patients. To judge the patient's progress an exercise test was used in which the subject walked over two steps 18 inches (45 cm.) high until pain was produced. In 10 patients observed over a period of several weeks during which no treatment was given the results of repeated tests on any one day remained fairly constant, although they were affected greatly by therapeutic suggestion, but those obtained on different days showed considerable spontaneous variation, occasionally as great as 45%; the coefficient of variation for the series was between 12 and 28%. These variations did not seem to be associated with changes in the rate of exercising. One patient who was given only inert preparations showed a marked spontaneous improvement continuing over several months.

In patients confined to bed, treatment by intermittent venous occlusion resulted in improvement, but the authors found that this improvement was no greater

than that which occurred in an initial period of bed rest or, in other cases, no greater in a treated as compared with an untreated limb which received the effects of bed rest alone. Intermittent venous occlusion unaccompanied by bed rest did not produce improvement. None of their patients treated with α-tocopherol, tolazoline (" priscol "), methyl testosterone, or dihydroergotamine showed any improvement in exercise tolerance which could be confidently regarded as due to the treatment. Lumbar sympathectomy was performed in only 2 cases in order to avert gangrene, which it successfully did. Tenotomy performed on 4 cases gave relief of pain in all, although in one case the disability from the operation was considered to be as great as that from the original complaint.

The effects of single doses of glyceryl trinitrite, adrenaline, nicotinic acid, tetraethylammonium bromide, tolazoline, dihydroergotamine and " padutin " were compared with that of a placebo. The patient performed an exercise test while the effect of the drug was at its maximum. No consistent improvement in exercise tolerance following administration of any of these drugs could be demonstrated.

It is emphasised that these results show the importance, in assessing the effects of a particular therapeutic regimen, of taking into account the considerable day-to-day variation in effort otlerance, the spontaneous improvement, and the beneficial effect of bed rest, which may occur in this disease. *Albert Venner*

1199. **Cerebrovascular Thrombosis in Patients with Buerger's Disease**
H. I. LIPPMANN. *Circulation* [*Circulation*] **5**, 661–692, May, 1952. Bibliography.

VEINS

1200. **Budd–Chiari's Syndrome: High Inferior Vena Caval Obstruction Demonstrated by Venography**
B. BRONTE-STEWART and R. H. GOETZ. *Angiology* [*Angiology*] **3**, 167–178, April, 1952. 7 figs., 12 refs.

The authors review the literature on Budd–Chiari's syndrome and discuss its aetiology and the possibility of a congenital predisposing factor.

They describe the case of a boy of 17 years who, when first seen, had lower substernal pain on effort. On examination he was found to be thin and poorly developed about the chest, neck, and arms, but well developed below the umbilicus; sexual development was retarded. The abdomen was distended and there was a small " caput medusae " in addition to a large vein passing up the right side of the abdomen in which the blood flowed towards the heart. The liver and spleen were enlarged, but there were no signs of hepatic insufficiency. The only other notable finding was a bilateral varicocele. Liver function tests were normal, and liver biopsy revealed only a slight increase in portal connective tissue. Glucose tolerance tests performed with blood taken from an antecubital vein and an abdominal-wall vein gave identical and normal results.

Venography of the inferior vena cava was performed, 50 ml. of 50% diodone being injected through a polythene tube inserted into the saphenous vein as far as its entry into the femoral vein. The inferior vena cava was dilated in its lower portion, and occluded high up in its intrahepatic course. The ascending lumbar, azygos, and inferior hemiazygos veins were also greatly dilated, as were a large number of additional venous channels. The dilated azygos vein formed a prominence on the right cardiac border at the point where it entered the superior vena cava, which could be seen on the plain radiograph of the chest.

The authors consider that venography is an important investigation which permits an exact diagnosis of this syndrome. They suggest that the discrepancy of body build, bilateral varicocele, and collateral abdominal veins in which the flow is from below upwards but which do not contain portal blood are important features not stressed by other workers. These features, together with hepato-splenomegaly and normal liver function, complete the picture of chronic hepatic vein obstruction.
J. F. Goodwin

1201. **Deep Venous Thrombosis in the Leg following Effort or Strain**
C. CRANE. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 529–533, April 3, 1952. 22 refs.

Deep venous thrombosis of the leg often occurs after gross injury. It also occurs after effort or strain without external trauma or joint or bone injury, but this condition has received comparatively little attention. A student entering Harvard University has to undergo a " step-up " test—that is, he has to step on to, and down from, an 18-inch (45-cm.) platform once every 4 seconds for 5 minutes; 4 cases of deep venous thrombosis due to exercise were observed.

The aetiology of the condition is discussed. It is considered that the great increase in pressure in the femoro–popliteal veins following forcible contraction of abdominal muscles causes a tear of one of the valves in the deep venous system; muscular contraction, particularly of the soleus muscle as it crosses the popliteal veins, is an additional factor in association with the acute venous hypertension. Essentially there is sudden pain in the limb with stiffness of the muscle, followed in 2 to 7 days by a diffuse oedema of the limb distally. At the same time there is some tenderness along the course of the vascular bundle. In a simple muscle strain, on the other hand, there may be some oedema, but this is localized and occurs usually within 4 to 24 hours; tenderness also is localized, not diffuse along the vascular bundle as is the tenderness resulting from venous thrombosis. It is probable that venous thrombosis following effort is fairly common, and that a significant proportion of the so-called idiopathic cases are due to effort or strain. A few days' rest with the limb elevated and administration of anticoagulants is all that is necessary for complete recovery without untoward sequelae.

The author describes 9 cases in detail.
Peter Martin

HYPERTENSION

1202. **A Study of Bilateral Total Adrenalectomy in Malignant Hypertension and Chronic Nephritis: Preliminary Report**
J. H. HARRISON, G. W. THORN, and M. G. CRISCITIELLO. *Journal of Urology* [*J. Urol.*] **67**, 405–413, April, 1952. 7 refs.

Total adrenalectomy was carried out in 14 patients with primary or renal hypertension with a view to eliminating substances resembling deoxycortone from the body and thereby avoiding excessive salt and water retention. The patients were maintained on a substitution regimen with limited salt and daily administration of cortisone, although some deoxycortone acetate was also necessary from time to time. Both adrenal glands were removed, preferably, at one operation, bilateral incisions being made through the twelfth rib bed.

The first results were encouraging; 9 patients survived operation, 7 of them being improved both subjectively and objectively. Severe renal impairment is a contraindication to total adrenalectomy.

J. Marshall Pullan

1203. **Adrenalectomy in Relation to Hypertension**
C. C. WOLFERTH. *Transactions and Studies of the College of Physicians of Philadelphia* [*Trans. Stud. Coll. Phys. Philad.*] **19**, 135–144, April, 1952. 25 refs.

The author presents a preliminary report on the use of adrenalectomy in the treatment of intractable hypertension. He states that it is necessary to remove at least 95% of adrenal tissue before any effect on blood pressure can be hoped for. When this is done symptoms of adrenal-cortical insufficiency may develop and require treatment. Adrenal insufficiency is nevertheless controllable and need not preclude attempts to influence hypertension by adrenalectomy.

Subtotal adrenalectomy alone has now been abandoned because of the disappointing results; a combination of the subtotal operation and a modified Adson type of sympathectomy has been used with success, blood pressure being reduced and symptoms relieved in very unpromising cases, including cases of cardiac failure. Severe renal disease is a contraindication.

J. Marshall Pullan

1204. **Hypertension and the Surgical Kidney**
A. D. PUPPEL and E. P. ALYEA. *Journal of Urology* [*J. Urol.*] **67**, 433–440, April, 1952.

The authors have studied the incidence and behaviour of hypertension coexisting with renal lesions in patients coming to nephrectomy and compared their findings with those in hypertensive patients without renal lesions.

In 23 of 67 patients with hypertension at the time of nephrectomy, which was performed for other reasons, blood pressure was normal two or more years after operation. This was most commonly seen after removal of a hydronephrotic kidney. The incidence of surgical renal lesions in hypertensive patients is only 2% and routine pyelograms are therefore considered not to be justified in hypertension. The incidence of hypertension is not significantly higher in patients admitted to hospital for surgical renal disease than in those admitted for other reasons.

J. Marshall Pullan

1205. **Control of Hypertension by Hexamethonium and 1-Hydrazinophthalazine. Preliminary Observations**
H. A. SCHROEDER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 523–540, April, 1952. 9 figs., 8 refs.

The author has treated empirically 40 patients suffering from hypertension of all degrees of severity with a combination of hexamethonium chloride and 1-hydrazinophthalazine. The former drug is a ganglionic blocking agent and the latter has been shown to antagonize most humoral pressor substances. Hospital in-patients who had failed to respond to dietary, surgical, or psychotherapeutic measures or to other drugs were selected for treatment, patients with severe renal insufficiency being excluded. Hexamethonium was given first in doses of 125 to 250 mg. by mouth every 8 hours; this was increased until a maximum of 500 mg. 4-hourly was reached or until the blood pressure fell intermittently to normal. In the most severe cases the drug was given intravenously, as an initial measure only. 1-Hydrazinophthalazine was then given orally to a maximum of 100 mg. 4-hourly or until the blood pressure was maintained " within normal limits "—that is, less than 140/90 mm. Hg, the blood pressure being recorded 4-hourly and the dosage adjusted accordingly. When a blood pressure of 140/90 mm. Hg had been maintained for a week the patient was discharged, but a modified regimen was continued at home, in which one night dose was omitted.

In ali the patients there was eventually a marked reduction in blood pressure. Of 20 patients with benign hypertension (blood pressure from 250/150 to 170/100 mm. Hg) normal pressure was attained in 14 and nearly normal in the other 6. Higher systolic levels were maintained deliberately in elderly arteriosclerotic patients. In 5 other patients with benign hypertension, on whom sympathectomy had been performed without success, a moderately hypertensive pressure (as measured supine) was maintained because of marked postural hypotension. In 13 out of 15 patients with malignant hypertension the malignant change was reversed; in 4 of these normal pressure was attained. Minor side-effects included constipation, disturbed vision, digestive disturbances, and retention of urine, but these gave trouble only during treatment of the malignant phase of the disease.

Objective improvements other than in the blood pressure were regression of retinopathy, disappearance of albuminuria, modest improvement in renal function, and relief of congestive cardiac failure. Subjective improvements were the disappearance of headache, palpitation, tinnitus, and exertional dyspnoea. The return of the blood pressure to normal was marked by a period of lassitude lasting 1 to 3 days; after that there was a marked return of strength and energy.

The hypothetical dangers of cerebral, coronary, and renal ischaemia from lowered blood pressure in hypertensive patients are discussed. The only noteworthy case

cited was that of a young patient with malignant hypertension who developed anuria and multiple myocardial infarction from a too rapid fall in blood pressure to a level of 110/70 mm. Hg.

[The longer-term follow-up of this series of patients will be awaited with interest.] *K. G. Lowe*

1206. **Discussion on the Medical Treatment of Hypertension**

M. L. ROSENHEIM and R. KAUNTZE. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **45**, 269–276, May, 1952. 11 figs., 13 refs.

Rosenheim, opening the discussion, reviewed the place of low-sodium diets and of hexamethonium in the treatment of essential hypertension. The Kempner rice diet, giving a daily intake of less than 200 mg. of sodium, or 500 mg. of salt, is effective in reducing blood pressure; headache is relieved, the heart decreases in size, and retinopathy diminishes. But patients rarely tolerate the diet for long, and improvement is only maintained while the diet is enforced.

Of the various drugs which have been recommended from time to time hexamethonium has proved the most effective. It acts by blocking impulses from the sympathetic ganglia and thus reduces blood pressure; but blocking of the parasympathetic impulses leads also to constipation, abdominal distension, dryness of the mouth, and even paralytic ileus. The drug can be given orally, or by subcutaneous, intramuscular, or intravenous injection. Absorption from the gut is poor and irregular, and about 10 times the parenteral dose is required. The subcutaneous dose varies widely, from 25 mg. daily to 250 mg. three times a day. Treatment is started by noting the effect of an intravenous injection of 25 mg. on the blood pressure. Then 25 to 50 mg. is given subcutaneously two or three times daily and the dose increased until the blood pressure is controlled. The patient should lie down for an hour after each injection to avoid postural hypotension. Daily blood-pressure readings with the patient recumbent and standing are taken 2 hours after an injection until the correct dose has been ascertained. In view of the rigorous nature of the treatment the drug should be reserved for patients with severe hypertension, such as those with marked retinal changes or nocturnal dyspnoea due to pulmonary oedema.

The discussion was continued by Kauntze, who considered the role of veratrum viride in hypertension. This drug causes hypotension, bradycardia, and emesis. In the form of "veriloid" it can be given orally or by intravenous injection. The initial oral dose is 8 mg. four times daily after meals; subsequent increases must be made cautiously, as the margin between the effective and toxic doses is small. Nausea and vomiting are also common when effective doses are reached. These disadvantages make it unlikely that the drug will find a permanent place in the treatment of hypertension outside hospital, except perhaps for younger patients. The results obtained in the treatment of 23 patients are reviewed and several case histories are given.

C. W. C. Bain

1207. **Effort Syncope as an Early Manifestation of Primary Pulmonary Hypertension**

W. DRESSLER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 131–143, Feb., 1952. 4 figs., 21 refs.

The author reviews 6 cases from the literature and describes 3 others in which syncope precipitated by effort was the chief sign of primary pulmonary hypertension. He states that this symptom combined with dilatation of the pulmonary artery, accentuation and splitting of the pulmonary second sound, and evidence of right ventricular hypertrophy, should suggest the diagnosis. Syncope may often occur before symptoms of congestive cardiac failure develop. Cyanosis is not an invariable feature of the condition. *G. S. Crockett*

PORTAL CIRCULATION

1208. **Portacaval Shunting for Portal Hypertension**

A. H. BLAKEMORE. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **94**, 443–454, April, 1952. 3 figs., 2 refs.

The author states that the value of the porta-caval shunt for portal hypertension is twofold: the operation lessens the danger of bleeding from oesophageal varices, and assists regeneration of damaged liver cells. He has estimated the portal pressure before and after anastomosis, and relates it to the behaviour of the oesophageal varices. At a postoperative pressure below 300 mm. of saline the varices disappeared or were lessened in a high proportion of patients, but in 12 of the 13 postoperative deaths from haematemesis the anastomosis was found to be occluded. He found this accident to be much less common when a direct-suture technique was used and when continuous local heparin was given after the operation.

He goes on to discuss operative risks in 166 operations on 160 patients; he believes these to be small where the block is extrahepatic and the liver normal. He considers in considerable detail the prognostic significance of many liver function tests. On the basis of these, plus clinical assessment, he divides the patients with intrahepatic obstruction into two groups: in the first—the "good risks"—mortality was 9·3%; whereas in the "bad risks" it was 39·9%. When the patients with extrahepatic obstruction are included the mortality for the entire series of 160 cases was 8·4%. The follow-up survival up to 7 years was in both groups over 80%. [These figures are most satisfactory, as the mortality from the disease untreated is of the order of 80% in the first year.]

J. R. Belcher

1209. **Lieno-renal Anastomosis: Results and Indications.** (Résultats et indications de l'anastomose spléno-rénale)

P. SANTY and P. MARION. *Mémoires de l'Académie de Chirurgie* [*Mém. Acad. Chir., Paris*] **78**, 296–301, March 12, 1952.

In this paper the indications for, and results of, splenorenal anastomosis are discussed. By means of operative exploration, liver-puncture histology, and portal veno-

graphy, it was possible to classify fairly accurately the cause of the portal obstruction. Of 53 patients operated upon, 18 had cirrhosis, 28 had extrahepatic portal obstruction, and 7 were unclassified. In 33 of the 53, spleno-renal anastomosis was performed by the technique of Blakemore and Lord, with postoperative death in 2 cases. In intrahepatic portal obstruction direct side-to-side portacaval anastomosis is preferred. Cases of alcoholic cirrhosis are operated upon only if recurrent haematemesis threatens life.

At operation, for which a left subcostal incision is used, portal angiography is performed. On the picture so obtained the decision whether to make a portacaval or spleno-renal anastomosis is taken. Of the 28 cases of extrahepatic portal obstruction, spleno-renal anastomosis was performed in 16, with one operative death. One patient had a postoperative retrograde mesenteric venous thrombosis, necessitating resection of 1·5 m. of intestine. Of 11 patients followed up for more than 2 years 8 had good results with cessation of haemorrhage; in the other 3 cases the anastomosis was probably thrombosed. In a further group of 8 cases the exact site of the block was not discovered and spleno-renal anastomosis was performed; in 2 of the 4 followed up for over a year the result was satisfactory. The high risk of operation in these patients is stressed; 5 patients are mentioned in whom for various reasons no form of anastomosis was possible and all of whom died. Unless, it is pointed out, this type of case is included in the statistics, a false idea of the mortality is obtained.

The role of the spleen in Banti's syndrome is also discussed. The fact that hypersplenism itself may contribute to the anaemia is an extra argument for removal of the spleen. *F. B. Cockett*

PERIPHERAL CIRCULATION

1210. **Local Circulatory Changes Associated with Clubbing of the Fingers and Toes**
G. M. Wilson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **21**, 201–213, April, 1952. 7 figs., 28 refs.

This investigation, from the University of Sheffield, was made to test the postulate that clubbing of the fingers and toes is primarily a manifestation of a peripheral circulatory disorder. The blood flow in the affected digits was measured by the heat-elimination method of Stewart, which involves the use of a calorimeter. The rate of blood flow compared with the available venous space was thought to be too great for the plethysmographic method to be accurate. To ensure that results on subsequent occasions, or from case to case, would be comparable, the patient was wrapped in blankets and the opposite limb immersed in water at 44° C. to produce full vasodilatation.

An increase of blood flow was demonstrated in cases of clubbing due to congenital heart disease, subacute bacterial endocarditis, and pulmonary disease. This increase of blood flow did not appear to be due to vasodilator nervous action as it was unaffected by procaine-induced nerve block. In 2 cases of unilateral clubbing due to arteriovenous fistulae the blood flow was greater in the affected than in the normal digits. A reduction of the circulation to the fingers led to a regression of the clubbing; this was shown in 2 cases in which the main artery to the limb was ligated. The regression in finger-clubbing seen after successful treatment of underlying thoracic disease was also associated with a decrease in blood flow.

The author discusses the relationship between the increased blood flow and the structural changes in the clubbed digits, and concludes that in unilateral cases clubbing is due to physical abnormalities in the arterial tree, while in bilateral cases " it is probably a result of generalized circulatory disturbance not yet fully understood ". *Albert Venner*

LYMPHATIC CIRCULATION

1211. **Lymphangiography in Man. A Method of Outlining Lymphatic Trunks at Operation**
J. B. Kinmonth. *Clinical Science* [*Clin. Sci.*] **11**, 13–20, 1952. 6 refs.

In investigations carried out at St. Bartholomew's Hospital, London, on animals, the author has studied 2 dyes, Evans blue (T 1824) and " patent blue V ", with the object of devising a means of demonstrating the flow in lymphatic trunks that might be used as a test for lymphatic patency in man. Both dyes were shown to be innocuous in doses much larger than those required for lymphangiography, but patent blue was considered to be more suitable for that purpose than Evans blue, which gave a heavy blue tinge to the skin which persisted in some animals for as long as 96 days. For clinical trial in man an 11% isotonic autoclaved aqueous solution of the dye was used, 2 or 3 ml. being injected into the sole of the foot subcutaneously or intramuscularly, or by both routes together, in 9 patients suffering from the late effects of thrombosis of the deep veins of the leg who were about to undergo exploration of the popliteal or femoral vein for phlebography or ligation. The injection was followed by a few minutes' massage of the foot and calf and the operation was then started. In the 7 cases in which patent blue was used the main lymphatic pathways were successfully outlined, and a true obstruction of the deep lymphatics at the ankle was demonstrated in a patient suffering from a long-standing circular ulcer of the ankle, in whom the popliteal lymphatics could be filled only by a second injection into the calf. Evans blue was used in 2 cases, but failed to outline the lymphatics in one, while in the other the leg was heavily stained for 3 weeks afterwards.

It was shown in the animal experiments that while a certain amount of time was required for the dye to enter the lymphatic channels, once it had done so its flow was remarkably rapid, even when the upper ends of the vessels were occluded by a tourniquet. This is difficult to explain unless it be presumed that the lymph trunks are initially empty or partly empty, with their thin walls collapsed. *Ian Aird*

Haematology

1212. **Hemophilia: Clinical and Laboratory Observations Relative to Diagnosis and Inheritance**
A. J. QUICK and C. V. HUSSEY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 401–413, April, 1952. 1 fig., 15 refs.

It is now generally accepted that the presence of five primary agents is essential for the formation of thrombin, namely, prothrombin, calcium, a labile factor, thromboplastinogen, and a platelet constituent. The chief diagnostic test for haemophilia has been the prothrombin consumption test. In this paper the authors describe a modification of that test which they call the " thromboplastinogen activity test ", and which they advocate as a supplement to the prothrombin consumption test when the diagnosis is in doubt.

The thromboplastinogen activity test is based on the observation that when rabbit-brain extract is heated to 60° C. or higher it loses its thromboplastic activity (for example, it no longer corrects faulty prothrombin consumption in haemophilic plasma), but it retains its potency to promote consumption of prothrombin in normal plasma from which platelets have been removed by centrifugation. Heated rabbit-brain extract thus behaves like a platelet extract. On the basis of this finding, the prothrombin consumption test is made more specifically a test for thromboplastinogen by adding a small quantity of heated rabbit-brain extract to blood before clotting. After a short period of incubation the serum is separated and tested for prothrombin. The prothrombin time of serum from thrombocytopenic blood is similar to that of normal serum, whereas the test described will detect low prothrombin consumption even in extremely mild cases of haemophilia.

A. Brown

1213. **Effect of Therapy on Blood Volume, Blood Pressure, and Spleen Size in Polycythemia Vera**
T. C. PRENTICE, N. I. BERLIN, and J. H. LAWRENCE. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 584–590, April, 1952. 1 fig., 8 refs.

Serial blood volumes were determined in 20 patients with polycythaemia vera, the majority of whom received ^{32}P; others received ^{90}Y and, in some cases, underwent phlebotomy as well. The blood-volume changes during treatment were estimated with ^{32}P-labelled erythrocytes, this being considered a more reliable method than the dye method. Results showed that with adequate treatment blood volume fell, and that in half the cases there was a parallel fall in total erythrocyte volume and plasma volume and in the other half a fall in total erythrocyte volume with a reciprocal rise in plasma volume. Both these patterns often appeared in the same patient at varying intervals. In the majority of instances changes in erythrocyte count and haematocrit value were parallel with changes in total erythrocyte volume. This did not, however, permit an accurate quantitative prediction of the change in total erythrocyte volume from changes in the haematocrit value or erythrocyte volume. A more satisfactory means of judging the response to treatment is by serial determination of the blood volume and of the total erythrocyte volume.

The incidence of hypertension in the authors' patients was 70%, whereas in another series of 154 patients it was 50%. Approximately one-third of the patients sustained a fall in blood pressure corresponding to a falling total blood volume, while in the other two-thirds the blood pressure remained the same or increased. No simple or constant relation between blood volume and pressure was demonstrated. The size of the spleen decreased rapidly and to a marked degree after treatment in all but one of the patients in whom it was originally palpable. The change in the size of the spleen did not appear to be a direct or simple function of the blood volume.

[The blood determinations were carried out for a period of just over a year. Lawrence has described the only large series of cases of polycythaemia vera treated with ^{32}P. This included 121 cases in which there were 24 deaths, 5 from leukaemia.] *Robert Hodgkinson*

NEOPLASTIC DISEASES

1214. **Treatment of Multiple Myeloma with Urethane. Experience with Sixty-six Cases over a Two-and-a-half-year Period**
W. F. LUTTGENS and E. D. BAYRD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **147**, 824–827, Oct. 27, 1951. 1 fig., 10 refs.

The authors give an account of the treatment of 66 cases of multiple myelomatosis with urethane (ethyl carbamate) over a period of 2½ years. At first urethane was given orally as a solution containing 0·5 g. per teaspoonful, and later as tablets each containing 5 gr. (0·3 g.). The amount given was the maximum tolerated by the patient, starting with 1·5 to 3 g. divided into three doses daily, and increasing by 0·5 g. every few days; 11 patients received urethane intravenously in a daily dose of 4 g. in 1,000 ml. of 5% solution of dextrose, and 7 patients were given urethane both orally and by the intravenous route.

About half the number of patients felt definitely better, but only a fifth were objectively improved. Increase in haemoglobin concentration and decrease in erythrocyte sedimentation rate were the most reliable signs of improvement. No changes in serum protein level, percentage of myeloma cells in the bone marrow, or *x*-ray appearances were noted; Bence Jones protein likewise did not disappear with treatment. Leucopenia occurred in the majority of patients but produced no

ill-effect, and in only 5 instances was treatment suspended on this account. Gastro-intestinal upsets were common. The authors conclude that although the results obtained with urethane are not very encouraging, it is probably as good treatment as is available at present for multiple myeloma. *R. Winston Evans*

1215. **On the Effect of Corticotropin (ACTH) on Myelomatosis with Special Reference to the Bone Marrow and the Serum Proteins.** [In English]
P. Effersøe, H. Gormsen, N. Harboe, S. E. Nielsen, and A. Videbaek. *Acta Medica Scandinavica* [*Acta med. scand.*] **143**, 63–82, May 10, 1952. 7 figs., 33 refs.

Corticotrophin prepared from pigs' pituitaries was given to 6 patients with multiple myelomatosis in courses of 10 units 5 times daily for 12 days. One of the patients had been treated with urethane just before, and another had a course of corticotrophin 1 year previously. The patients developed nausea and diarrhoea. Bone pain disappeared in all, but moderate oedema developed. Changes in body weight were not constant. During the course of treatment the excretion of neutral 17-ketosteroids rose and the eosinophils largely disappeared from the peripheral blood. Though the urea clearance did not change, the blood urea level often rose. In 2 patients the erythrocyte sedimentation rate fell markedly during treatment; in 4 the excretion of protein in the urine increased, though the excretion of Bence Jones protein decreased with treatment. The serum globulin level in the blood decreased during treatment and rose again afterwards. The composition of the bone marrow was repeatedly studied by sternal puncture, in smears and in histological preparations, but no changes were found either quantitatively or morphologically that could be attributed to the treatment with corticotrophin.
E. Neumark

1216. **Splenectomy in Leukaemia and Leukosarcoma**
J. H. Fisher, C. S. Welch, and W. Dameshek. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 477–484, March 27, 1952. 3 figs., 35 refs.

The rationale of splenectomy in cases of leukaemia and leucosarcoma is based on a consideration of the functions of this organ both as a site of haemolysis of old or abnormal erythrocytes and in the control of the numbers of circulating blood cells. Though the mechanism is not clear, the spleen may exert these controls on bone-marrow activity either by blocking the escape of mature cells into the blood stream or by retarding haematopoiesis. Accentuation of either function may be termed " hypersplenism " and gives rise to selective cytopenia or pancytopenia. Such hypersplenism, which may be idiopathic or secondary in origin, may occur in leukaemia or leucosarcoma, especially in those cases with an accompanying splenomegaly.

The case histories of 18 patients with leukaemia or leucosarcoma who underwent splenectomy at the New England Center Hospital, Boston, are given in detail. The operation was undertaken to relieve one or more of the following: haemolytic anaemia, pancytopenia, thrombocytopenia, and splenomegaly with severe pain. In 11 cases there was some degree of improvement, and 8 of these patients experienced prolonged relief of their symptoms. The authors conclude that in carefully selected cases splenectomy may be of palliative value in leucosarcoma and leukaemia, although the primary condition is not influenced. *H. Payling Wright*

1217. **The Topographical Distribution of Leukemia and Hodgkin's Disease in Denmark 1942–46.** [In English]
J. Clemmesen, T. Busk, and A. Nielsen. *Acta Radiologica* [*Acta radiol., Stockh.*] **37**, 223–230, March–April, 1952. 8 figs., 4 refs.

1218. **Resistance to Corticotropin, Cortisone, and Folic Acid Antagonists in Leukemia**
E. M. K. Pillers, J. H. Burchenal, L. P. Eliel, and O. H. Pearson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 987–994, March 22, 1952. 4 figs., 12 refs.

At the Sloan-Kettering Institute, Memorial Cancer Center, New York, a series of 16 children (Series A) were treated with corticotrophin (50 to 100 mg. per day) or cortisone (100 to 400 mg. per day) after cessation of response to folic acid antagonists; a further series of 6 children (Series B) were treated with folic acid antagonists (mainly " amethopterin ") after they had ceased to show response to corticotrophin or cortisone. Of the 16 patients in Series A, 10 showed a good clinical and haematological response. In Series B a good response was obtained in 3 patients. The authors suggest that their results point to the fact that the hormones and folic-acid antagonists have a different primary effect on the leukaemic processes, and that remissions can be induced in about 50% of patients by alternate therapy.
R. Winston Evans

ANAEMIA

1219. **The Haematological Consequences of Gastric Resection.** (Il danno ematologico nei gastro-resecati)
M. Banche. *Minerva Medica* [*Minerva med., Torino*] **43**, 645–656, March 29, 1952. 2 figs., bibliography.

At Turin City Hospital 56 patients who had undergone gastrectomy were examined and reviewed in the two years 1949 and 1950. The blood, bone marrow, and gastric contents were investigated, and the stomach was examined radiologically and in many cases also by gastroscopy. Over 60% of the patients were anaemic, in most cases owing to haemorrhage. Anaemia was mostly normochromic and usually normocytic; macrocytosis was present in about one-third. Free hydrochloric acid was found in the stomach of 21 patients. The number of reticulocytes was not increased, and the sedimentation rate and osmotic fragility of the erythrocytes were usually normal. The number of leucocytes was reduced in one-third of the patients, particularly in women, but this was not related to the degree of anaemia. In 28 patients the bone marrow was examined. Maturation curves of erythroblasts showed a lag in over 50%,

and maturation curves of myeloid cells showed a lag in 76%. The author concludes that gastrectomy, by removing an organ which has a definite influence on the regulation of haematopoiesis, induces "haematological instability", and that the accompanying anaemia is mostly due to prolonged, though often slight, bouts of haemorrhage. *E. Neumark*

1220. **The Occurrence of Pernicious Anemia and Polycythemia in the Same Patient.** [In English]
A. P. SKOUBY. *Acta Medica Scandinavica* [*Acta med. scand.*] **141**, 244–248, Jan. 25, 1952. 1 fig., 16 refs.

1221. **Megaloblastic Anaemia in Young Adults. Aetiological Importance of Occult Idiopathic Steatorrhoea**
H. CONWAY. *British Medical Journal* [*Brit. med. J.*] **1**, 1098–1102, May 24, 1952.

Because of the rarity of true pernicious anaemia in patients under the age of 30 the author re-examined 7 patients in whom pernicious anaemia had been diagnosed before the age of 30 in the period 1937–49. Of the 7 patients 4 were found to be suffering from steatorrhoea, although none had had any significant intestinal symptoms; originally all 4 had histamine-fast achlorhydria, which probably accounted for the diagnosis of pernicious anaemia. Of 3 of these patients who had never responded well to parenteral liver extract and were still anaemic in 1950, 2 responded well to folic acid, while the third required, in addition, a proteolysed liver preparation.

It is suggested that in the presence of achlorhydria the next most important points in the differential diagnosis are the failure to respond adequately to parenteral liver preparations, the low sugar-tolerance curve, and, of course, the 4-day fat-excretion rate, which is always increased in steatorrhoea and should indicate treatment with folic acid. *R. F. Jennison*

1222. **Genetic Aspects of Sickle Cell Anemia and Microdrepanocytic Disease**
E. SILVESTRONI and I. BIANCO. *Blood* [*Blood*] **7**, 429–435, April, 1952. 4 figs., 17 refs.

The authors report an extension of their previous work, published in Italy, on the clinical manifestations found in individuals who have inherited the sickle-cell factor from one parent and the microcythaemic (Mediterranean anaemia) factor from the other parent. The combination of the two factors results in microdrepanocytic disease which, clinically, resembles severe sickle-cell anaemia. The condition can be recognized by blood studies. Gross hypochromia with target cells and extreme poikilocytosis, some cells being sickled, occur in the stained film.

It has been suggested that: (1) the genes for sickling and for microcythaemia are on different chromosomes and are inherited independently; (2) the disease is an extreme variant of one or other of the two diseases, the gene for the other being present without effect; or (3) the two genes are members of a series of multiple allelomorphs. The evidence from the 11 families studied supports the first hypothesis, namely, that the two diseases are determined by factors on two different autosomes. *George Discombe*

1223. **Paroxysmal Nocturnal Hemoglobinuria. A Clinicopathological Correlation**
R. R. MERLISS. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 642–646, April 24, 1952. 1 fig., 18 refs.

This is a report of 2 cases of paroxysmal haemoglobinuria which the author has observed personally over a number of years. One of these patients has since died, death being attributed to massive haemorrhage into the urinary tract; at necropsy both kidneys had an unusual brown colour from haemosiderin deposits in the tubular epithelium. The author emphasizes the anhaemoglobinuric phases of this disease, in which, however, active haemolysis is still present, as indicated by an elevated icterus index, an abnormally high reticulocyte count, and a falling erythrocyte count. Haemoglobinuria may be provoked by intercurrent infection, or by taking ammonium chloride or aspirin. It is related to the physiological fall in the *p*H of the serum during sleep. Blood transfusion has a spectacular, if temporary, effect on the progress of this rare blood dyscrasia, as the erythrocytes introduced are resistant to the haemolysing factors. Thrombosis is suggested as a cause for the bouts of upper abdominal pain which occurred. Leucopenia may be related to the non-specific splenomegaly which was present, but splenectomy in one of these cases did not influence the progress of the disease. *E. T. Ruston*

1224. **The Mechanism of Hemolysis in Paroxysmal Cold Hemoglobinuria. III. Erythrophagocytosis and Leukopenia**
W. S. JORDAN, R. L. PROUTY, R. W. HEINLE, and J. H. DINGLE. *Blood* [*Blood*] **7**, 387–403, April, 1952. 3 figs., bibliography.

The haematological changes occurring in paroxysms of cold haemoglobinuria were studied in 2 patients. Haemolysis was maximal about 15 minutes from the start of chilling, and at this time there was marked leucopenia of all elements except atypical mononuclear cells. Urinary haemoglobin excretion was maximal after 60 to 70 minutes. During the period of maximum haemolysis neutrophil and mononuclear leucocytes showed marked erythrophagocytosis, up to 65% of neutrophils and 10% of monocytes containing erythrocytes.

Experiments *in vitro* showed that erythrophagocytosis was dependent on: (1) the presence of complement; (2) sensitization of the phagocytosed cells by a suitable antibody, either that of paroxysmal cold haemoglobinuria or a normal isohaemagglutinin; and (3) a temperature at which leucocytes were active. Erythrophagocytosis was observed directly in hanging-drop preparations; leucocytolysis did not occur. The authors conclude that the erythrophagocytosis is probably a means of removing damaged erythrocytes from the blood; and that the leucocytes which ingest these cells are probably trapped in the capillaries of various organs.
George Discombe

Respiratory System

1225. **Hemopneumothorax: Re-evaluation of Treatment**
G. A. Beatty and R. W. Frelick. *Annals of Internal Medicine* [*Ann. intern. Med.*] **36**, 845–851, March, 1952. 13 refs.

The authors review the management of spontaneous haemopneumothorax in the light of their experience in the treatment of 7 cases at the Memorial Hospital, Wilmington, Delaware. They recommend the following measures: (1) prompt aspiration of both blood and air to facilitate re-expansion of the lung; (2) blood transfusion to restore blood volume; (3) in cases of uncontrollable bleeding early thoracotomy is necessary for the evacuation of the blood and manual removal of clots; (4) the intrapleural use of streptokinase and streptodornase to reduce clot formation in the chest; (5) early pulmonary decortication when an organizing haemothorax is interfering with re-expansion.

[Thoracoscopy, which can be of so much diagnostic and therapeutic help in the management of haemopneumothorax, is not mentioned in this paper.]

A. I. Suchett-Kaye

1226. **Practical Value and Limitations of Respiratory Function Tests**
R. D. Berke, S. J. Presley, J. R. Necheles, J. R. Scala, A. Wolf, and M. Samter. *Journal of Allergy* [*J. Allergy*] **23**, 151–162, March, 1952. 10 figs., 6 refs.

In 83 patients suffering from seasonal or perennial asthma the vital capacity and maximum breathing capacity were estimated before and after the administration of either 0·3 mg. adrenaline, or 50 mg. diphenhydramine, or 250 mg. aminophylline. With adrenaline there was improvement in all cases, diphenhydramine improved only the cases with seasonal asthma, and aminophylline had little effect. The authors are aware of the limitations of the methods used.

H. Herxheimer

1227. **Clinical Significance of Hemoptysis**
H. J. Moersch. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1461–1465, April 26, 1952. 5 figs.

Haemoptysis is always alarming, and demands the fullest investigation; when causes such as active tuberculosis, mitral disease, pneumonia and bronchiectasis have been excluded the commonest source of bleeding is a bronchial carcinoma in those over 40 years of age and bronchiectasis in those under that age.

Two points of clinical interest are that in 4 of the author's 200 patients with haemoptysis at the Mayo Clinic the bleeding probably came from a pulmonary metastasis, although the exact nature of the lesion could not be established and the patients refused operation; and that in 17 patients he could find no cause for the bleeding. He concludes that when no cause is found after due and proper search " there is an excellent chance that a serious pulmonary lesion will not develop subsequently ".

Maxwell Telling

LUNGS AND BRONCHI

1228. **Pulmonary Surgical Salvage by Bronchial Resection**
P. W. Gebauer. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **94**, 347–357, March, 1952. 9 figs., 14 refs.

It is not always necessary to sacrifice a lobe or whole lung if there is a lesion of the supplying bronchus that requires removal. Although in many cases of stricture or benign tumour changes have occurred in the peripheral lung that require removal of both lung and bronchus, there are occasions when a local repair or reconstruction of the air tube would obviate the removal of valuable pulmonary tissue. Tuberculosis of the bronchial tree is a fruitful source of cases in which this " surgical salvage " of lung may be achieved by methods varying from resection and end-to-end junction of a main bronchus to the use of a wire-supported skin graft to fill in a gap. With a narrow stricture or small tumour a sleeve resection will suffice, but where a wide or irregular deficiency is produced a graft will be required. Five cases are reported in which one or other of these methods was adopted and the lung saved.

T. Holmes Sellors

1229. **Cystic Sequestration of the Lung Associated with an Abnormal Artery Arising from the Aorta, with Reference to Six Cases.** (La séquestration pulmonaire kystique avec artère anormale d'origine aortique à propos de six cas)
P. Santy, M. Bérard, P. Galy, and N. Huu. *Journal Français de Médecine et Chirurgie Thoracique* [*J. franç. Méd. Chir. thorac.*] **6**, 101–139, 1952. 12 figs., bibliography.

The authors describe in detail 6 patients, each of whom had an intralobar cystic area of lung tissue in one or other lower lobe, occupying the postero-inferior part of the lobe and usually readily separable from the rest of it. This cystic area of sequestration received from the thoracic aorta an abnormal blood supply which seemed to be derived from persisting embryonic connexions between the aorta and the post-bronchial pulmonary plexus of Huntington. Previously reported cases of similar anatomical anomalies are discussed, together with theories that have been put forward to explain their formation. It has been suggested that such cystic sequestration is the result of the arterial abnormality, and that the majority of congenital cysts of the lungs are produced in this way.

Many such cystic malformations remain latent, giving rise to no symptoms, but infection at some time or another

is common. When this happens the clinical picture may be confused with such conditions as bronchiectasis, lung abscess, encysted empyema, pyopneumothorax, pneumonia, or tuberculosis. However, if the cystic condition is correctly diagnosed surgical removal is indicated, but the surgeon should bear in mind the probable existence of abnormal arteries in the neighbourhood.

John R. Forbes

1230. **Cerebral Circulation and Metabolism in Chronic Pulmonary Emphysema. With Observations on the Effects of Inhalation of Oxygen**

J. L. PATTERSON, A. HEYMAN, and T. W. DUIE. *American Journal of Medicine* [*Amer. J. Med.*] **12**, 382–387, April, 1952. 4 figs., 15 refs.

In experiments carried out at Emory University School of Medicine and Grady Memorial Hospital, Atlanta, Georgia, the authors found that inhalation of oxygen increased the cerebral blood flow (measured by the nitrous oxide method of Kety and Schmidt (*J. clin. Invest.*, 1948, **27**, 484)), lowered the cerebral vascular resistance, and increased the cerebrospinal-fluid pressure in a series of 9 patients suffering from emphysema. These changes did not occur in a control series of 8 normal subjects. The cerebral oxygen consumption did not appear to be altered in either group. The changes were related directly to the partial pressure of carbon dioxide, and inversely to that of oxygen, in the arterial blood.

[The fact that the control subjects' average age was 30, whereas that of the patients was 50 years, vitiates the conclusion that these changes are specific to persons suffering from emphysema.] *J. Robertson Sinton*

1231. **Circulatory Changes in Severe Pulmonary Emphysema**

J. P. D. MOUNSEY, L. W. RITZMANN, N. J. SELVERSTONE, W. A. BRISCOE, and G. A. MCLEMORE. *British Heart Journal* [*Brit. Heart J.*] **14**, 153–172, April, 1952. 10 figs., 33 refs.

An investigation was carried out at the Postgraduate Medical School of London on 24 patients with severe pulmonary emphysema, which was diagnosed clinically and by the finding of a gross reduction in maximum breathing capacity, increase in the residual air, and decrease in the "90% helium mixing index". On cardiac catheterization right ventricular systolic pressures were found to be normal or only moderately raised in patients without congestive heart failure, but were raised in every patient suffering from congestive failure; these pressures gradually fell during recovery towards normal levels. End diastolic pressures were also consistently raised only in the presence of congestive failure.

Since pulmonary hypertension is reversible in emphysema with congestive cardiac failure, it cannot be the result of permanent structural changes in the arterial bed. Anoxia has been suggested as a possible cause, and there was some correlation in this series between arterial oxgen non-saturation and pulmonary hypertension, but its correction by oxygen administration did not consistently produce a fall in pressure. Exercise produced a rise in right ventricular systolic pressure in patients with severe emphysema, whether in failure or not, but not in normal controls, and it is possible that a reduction in the pulmonary vascular bed may be sufficient to produce hypertension when combined with an increased blood volume in cardiac failure, but there was no correlation between cardiac output and pulmonary hypertension. The immediate effect of full doses of "digoxin" or "ouabain" (strophanthin-G) were observed in 5 patients. No change in cardiac output occurred, but right ventricular pulse pressure was increased, with a lower diastolic filling pressure, these changes suggesting some improvement in myocardial function.

J. W. Litchfield

1232. **An Effective and Economical Method for the Treatment of Acute Nontuberculous Bacterial Pneumonia**

L. V. MCVAY and T. N. STERN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **2**, 215–220, April, 1952. 11 refs.

The authors report the successful treatment of acute non-tuberculous pneumonia at the John Gaston Hospital, Tennessee, with comparatively small doses of aureomycin. They point out that pneumonia still remains a serious hazard in old age. Despite intensive antibiotic and sulphonamide therapy there were 34 deaths from pneumonia in their hospital in 1950. Of these fatal cases, in 8 of pneumococcal pneumonia the average age was 67·4 years, while in 26 fatal cases of non-pneumococcal pneumonia the average age was 66·9 years.

The authors set out to find a scheme of dosage and administration of aureomycin which would be suitable for the treatment of aged patients in their own homes. They found that 250 mg. of aureomycin administered orally 4 times daily gave blood concentrations of 16 to 0·25 μg. per ml. This dosage was used in the treatment of 74 cases of pneumonia, 29 of which were pneumococcal. Of the remaining 45 patients, 23 were over 50 years of age, and 9 of these were critically ill on admission. Sputum cultures yielded a variety of organisms in this group, including *Micrococcus pyogenes* var. *aureus*, streptococci, and Gram-negative bacilli. Blood culture was positive in 2 cases, from one of which Friedländer's bacillus was isolated. Many patients had complicating conditions such as hypertensive disease, pyelitis, and bronchiectasis.

The results of treatment in the two groups were found to be uniformly good. There were no deaths. Empyema developed in one case in each group. In the non-pneumococcal case a coagulase-negative *M. pyogenes* var. *aureus* was isolated from the aspirated pus. The empyemata were treated by chest aspiration and instillation of 1,000,000 units of penicillin; surgical intervention proved unnecessary.

The authors used a preparation of aureomycin containing mixed paraben esters which control the incidence of moniliasis. They claim that spacing out the dosage as described reduces the incidence of gastro-intestinal side-effects. They consider that this form of therapy is well adapted to the treatment of pneumonia in the patient's home. *William Hughes*

Otorhinolaryngology

1233. **Suppurative Labyrinthitis**
G. E. ARCHER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **45**, 121–127, March, 1952.

This review is based on 1,379 operations performed by the author for suppurative conditions of the middle ear, 767 during the period 1921–36 (before the introduction of sulphonamides), 409 in 1937–45 (the chemotherapy period), and 203 in 1946–51 (the antibiotic period). Although there was a decline in the frequency of meningitis and sinus thrombosis throughout the period, the incidence of labyrinthitis does not show the same trend: out of 157 cases of labyrinthitis of all types, 59, 52, and 46 respectively fell within each of the above periods. It was considered necessary to operate on the labyrinth in 52 of these cases, 4 of which proved to be due to malignant disease. Of the remaining 48 patients, 12 (6 with acute and 6 with chronic infection) also had meningitis and were subjected to translabyrinthine drainage, only one surviving. The author would now reserve this treatment for those cases which fail to respond to chemotherapy and antibiotics, but since the advent of antibiotics he has had no case of meningitis associated with labyrinthitis.

When acute suppurative labyrinthitis and meningitis develop in cases of acute suppurative otitis media the symptoms of the former complication are masked by those of the latter, and it is impossible to say whether they arise concomitantly or whether the meningitis is secondary to the labyrinthitis. In cases of chronic suppurative otitis media spread of the disease to the labyrinth may take place and the function of the labyrinth may be completely destroyed without there ever having been symptoms of labyrinthine dysfunction (latent labyrinthitis); alternatively, such symptoms may precede loss of function (manifest purulent labyrinthitis). The latter type of case should be treated with heavy doses of antibiotics, and labyrinthotomy should be performed at the first sign of meningitis. In latent labyrinthitis the author would now operate to drain the infected middle-ear tract, and would proceed to drain the labyrinth only if pus were seen coming from the labyrinth. In cases of serous labyrinthitis where there are intermittent attacks of labyrinthine irritation followed by partial or complete recovery of function the decision whether to treat by adequate drainage of sepsis in the middle ear alone or by labyrinthotomy in addition will be determined by the severity and frequency of the attacks of vertigo, the presence or absence of deep-seated pain and creamy pus, and the response to antibiotics. Cases of circumscribed labyrinthitis usually heal after radical (or modified) mastoid operation.

In general, the tendency nowadays is to be more conservative in treating all types of labyrinthitis.

Norman W. MacKeith

1234. **Psychosomatic Aspects of Ménière's Disease**
E. P. FOWLER and A. ZECKEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1265–1268, April 12, 1952. 3 figs., 17 refs.

As a result of their investigations into the aetiology of Ménière's disease the authors come to the conclusion that the disease is caused by vascular phenomena in the labyrinth due to emotional stimuli. They examined 23 patients suffering from paroxysmal vertigo with nausea and vomiting, tinnitus, and hearing loss in at least one ear. The majority were found to be extroverts of aggressive appearance and temperament. Although anxiety may have contributed to some attacks, the real psychological disturbance appeared to be more deep-seated. Symptoms of Ménière's disease could be induced experimentally by emotional stimuli, and the authors conclude that a certain predisposed personality may react to stress in this way.

As a result of disturbances in autonomic control certain vascular phenomena are produced in the inner ear which may lead to the pathological change of hydrops of the labyrinth. After the liberation of adrenaline, vasospasm and slowing of the circulation occur, which cause clumping of erythrocytes and may be associated with microscopic haemorrhages. This phenomenon of intravascular "sludging" was also observed in the conjunctival vessels after experimental emotional stimuli. Procaine given intravenously counteracted these changes and was found to stop or modify the tinnitus during attacks of Ménière's disease.

The authors conclude that Ménière's disease should be regarded as a psychosomatic disorder. In the early stages psychotherapy may arrest the disease, and as patients tend to be of a similar personality pattern, group treatment may be practicable.

G. E. Stein

1235. **An Investigation into the Relationship between Adenoids and Sinusitis in Children**
P. H. HUGGILL and J. C. BALLANTYNE. *Journal of Laryngology and Otology* [*J. Laryng.*] **66**, 84–91, Feb., 1952.

The authors report on a series of 55 children complaining of nasal obstruction and repeated colds and suffering from the combined lesions of adenoids and sinusitis. Investigation consisted in: (1) eliciting a detailed history; (2) the taking of a lateral radiograph of the nasopharynx; and (3) antral lavage with bacteriological examination of the washings. Adenoidectomy was then performed.

The authors conclude that when adenoids and antral infection are present together, removal of the adenoids should alone be carried out in the first instance, as this leads to cure in most cases; the antra should be treated only if symptoms persist for 3 to 6 months after operation.

H. D. Brown Kelly

Urogenital System

KIDNEY AND URETER

1236. **Pyelonephritis Lenta**
O. SAPHIR and B. TAYLOR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **36**, 1017–1041, April, 1952. 16 figs., 20 refs.

In 43 out of 50 cases of malignant hypertension with terminal uraemia, seen at necropsy, the kidney was the seat of unmistakable and severe chronic pyelonephritis; in 3 cases the pyelonephritis was slight and combined with arteriosclerosis and arteriolosclerosis; in 3 there was acute pyelonephritis; and in one case arteriosclerosis and arteriolosclerosis only were observed. The average age of the patients was 47 years, and of a control group in which death was due to complications other than uraemia it was 65.

A history suggestive of pyelonephritis had seldom been obtained from the uraemic patients. The average blood pressure was 227/133 mm. Hg, compared with 180/102 mm. Hg in the control group. The biochemical findings in the two groups could not be compared as the recording of these was not consistent. Pathological and histological findings, however, were collected under identical conditions. In the uraemic group the average weight of both kidneys was 244 g., compared with 322 g. in the control group, and there was often considerable difference in size; capsules stripped off with difficulty, scars were observed fairly frequently, as were petechiae and/or haemorrhages; there was dilatation of the pelvis, with thickening of the mucosal lining and flattening of the pyramids. The criteria adopted on microscopical examination for a definite diagnosis of chronic pyelonephritis were: the presence of interstitial infiltration, tubular changes, glomerular lesions, chronic pyelitis and renal capsular scarring, and vascular lesions. The findings varied and there was not always a uniform pattern of changes, but a definite histological diagnosis of pyelonephritis could be made in all cases.

The authors consider that the unsatisfactory term " malignant hypertension " should be discarded in favour of " pyelonephritis lenta ". *L. H. Worth*

1237. **Atrophic Pyelonephritis versus Congenital Renal Hypoplasia**
J. L. EMMETT, J. J. ALVAREZ-IERENA, and J. R. MCDONALD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **148**, 1470–1477, April 26, 1951. 6 figs.

The authors have reviewed the clinical records of 400 patients with a unilateral small kidney; the selection was made from a total of 5,000 patients admitted to the Mayo Clinic between 1935 and 1948 with a variety of diagnoses such as chronic pyelonephritis and atrophic kidney. The object was to trace possible aetiological factors and to determine whether a distinction between congenital hypoplasia and atrophic pyelonephritis was justifiable. Of the 400 patients, after the exclusion of cases of atrophy due to obstruction, 183 had had a small kidney (less than 100 g.) without apparent reason, and these were selected for study; included were 3 children under 10 with proportionately small kidneys. Most of the patients were between the ages of 21 and 50, and two-thirds were women. They were subdivided into those with evidence of urinary infection (115) and those without (68).

The commonest manifestations were renal pain and hypertension. Hypertension (taken as a blood pressure greater than 150/100 mm. Hg) was present in 32% of those with urinary infections and in 46% of those without infection; renal pain was present in about 50% of all patients. Renal function on the affected side (that is, in the small kidney), estimated by excretion urography, was poor or absent in only 42%.

In the 79 cases of this series in which nephrectomy had been performed pathological examination of the specimens removed at operation showed that they could be classified into: (1) those in which the kidney consisted of a mass of fibrous tissue (aplasia, 6); (2) kidneys in which a few glomeruli were recognizable (hypoplasia, 9); (3) those in which there were scarred areas, dilatation of the tubules, and round-celled infiltration (chronic pyelonephritis, 51); and (4) kidneys presenting a mixed picture of hyperplasia and pyelonephritis (13). There was no correlation between the pyelographic appearances and the type of lesions found, nor did there appear to be any correlation between the degree of renal atrophy or type of lesion and the severity of hypertension. Immediate relief of hypertension (blood pressure falling below 150/100 mm. Hg) followed nephrectomy in 22 of 43 patients, and the result of operation has remained good for 2 years in 19, the blood pressure rising again to above 150/100 mm. Hg in the other 3. There was no apparent correlation between the duration of symptoms before operation, the age of the patient, or the degree of renal atrophy and the quality and duration of relief after nephrectomy.

It is concluded that both congenital renal aplasia and acquired renal atrophy without apparent cause exist, but that it is not practicable to distinguish the two conditions clinically, pathologically, or urographically with any degree of accuracy. Infection appears to be an important aetiological factor in the acquired variety of small kidney. *Charles P. Nicholas*

1238. **Wilms's Tumor in an Adult. First Reported Case Found Incidentally at Autopsy**
E. V. OLMSTEAD. *Cancer* [*Cancer*] **5**, 324–327, March, 1952. 5 figs., 43 refs.

1239. **Acute Glomerulonephritis in Childhood. A Study of the Late Prognosis of Twenty-seven Cases**
H. J. HEBERT. *Journal of Pediatrics* [*J. Pediat.*] **40**, 549–557, May, 1952. 38 refs.

The author has attempted to discover the relation, if any, between acute nephritis in childhood and chronic nephritis in later life.

Of 200 children with acute glomerulonephritis who were seen at the Children's Memorial Hospital, Chicago, between 1917 and 1932 the author was able to trace 27, one of whom had already died. The acute illness in these patients had occurred between the ages of 2 and 12 years; at the time they were traced they were between 26 and 41 years of age.

The author found that in 17 patients blood pressure was normal, 19 had no albuminuria, while 16 showed no urinary sediment. The remaining 7 patients were not examined. Many of the patients had no recollection of their childhood illness.

[Since only a very small number of the original patients were traced, any conclusions from this study would be unwarranted.] *G. Loewi*

1240. **Infiltration of the Renal Peduncle with Procaine in the Treatment of Nephritis.** (La novocainizzazione del peduncolo renale nella nefrite)
A. TREVISINI. *Urologia* [*Urologia, Treviso*] **19**, 71–90, Feb. 20, 1952. 7 figs., 15 refs.

The effect of infiltration with procaine of the renal peduncle in 43 patients suffering from acute or subacute glomerulonephritis (17), chronic nephritis or nephrosclerosis (18), mercuric chloride poisoning (1), or pyelonephritis (7) is reported. Of the first group only 2 were not cured within the follow-up period. [This percentage corresponds with the figures which have been published in Britain since Ellis's original paper in 1942.] Among the patients of the second group, 9 also suffered from oliguria or anuria of a few days' duration, and 2 of these seem to have benefited from the treatment, while all those without oliguria showed less albuminuria after the infiltration; the same was true for the group with pyelonephritis. *L. H. Worth*

See also Cardiovascular System, Abstracts 1202–3.

1241. **Lipoid Nephrosis and its Treatment with ACTH (Corticotrophin).** (La nefrosi lipoidea ed il suo trattamento con ormone corticotropo (A.C.T.H.)
W. TANGHERONI and E. BOTTONE. *Rivista di Clinica Pediatrica* [*Riv. Clin. pediat.*] **50**, 145–161, March, 1952. 3 figs., 28 refs.

The authors review modern ideas on the aetiology and mechanism of nephrosis and the part played by endocrine glands in this disease, and summarize the favourable reports on corticotrophin therapy in recent American literature. They then describe the case of a 5-year-old child who developed a fever and cough, followed in a few days by oedema, oliguria, and albuminuria. On admission to hospital he presented the classical picture of nephrosis, with generalized oedema, gross albuminuria, low plasma protein and high lipid contents, and a hypochromic anaemia. He was treated during the first month with penicillin and thyroid, but his condition steadily deteriorated and it was decided to try the effect of corticotrophin. He was given 36 mg. daily for 3 days, followed by 48 mg. daily for a further 8 days, after which the drug was stopped abruptly.

Though there was some improvement in well-being during treatment, there was only a slight increase in urinary output, and some reduction in the oedema and albuminuria after stopping the drug. Extensive investigations were carried out during the period of observation, but apart from demonstrating the metabolic activity of corticotrophin they failed to show any significant effect on the nephrotic picture itself. The patient continued to deteriorate and abdominal paracentesis became necessary. After a further month corticotrophin (48 mg. daily for 10 days) was again given, but the response was negligible; soon afterwards the patient was discharged at the request of the parents. The authors conclude that the value of corticotrophin in the treatment of nephrosis is as yet unproven.

[For details of the biochemical findings the original paper should be consulted.] *A. Paton*

1242. **Some Effects of Cortisone on Metabolic Disturbance Associated with Renal Edema**
N. M. KEITH, M. H. POWER, G. W. DAUGHERTY, and H. M. KEITH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 689–707, May, 1952. 9 figs., 47 refs.

Metabolism was studied in 3 patients suffering from renal oedema of the nephrotic type who were receiving cortisone. There was an increase in catabolism accompanied by an increase in oedema during the early stages of treatment; this was followed by a diuresis and loss of oedema in 2 patients. In one patient proteinuria disappeared. *G. M. Bull*

1243. **Role of Protective Urinary Colloids in Prevention of Renal Lithiasis**
A. J. BUTT. *Journal of Urology* [*J. Urol.*] **67**, 450–459, April, 1952. 3 figs., 17 refs.

The author discusses the formation of renal calculi, defining a calculus as " a concretion of urinary crystalloids bound together by a colloidal matrix ". He points out that the influence of the colloids in the aetiology of stone has not been adequately investigated, attention having in the past been concentrated on the crystalloids. Urinary colloids increase the solubility of stone-forming salts; other factors, such as the temperature and reaction of the urine, have a marked influence on the nature of the deposit, but none in preventing its formation. Concentration of the urine increases the proportion of electrolytes and decreases that of colloids, thereby increasing the possibility of precipitation. Thus exposure of the body to dry heat is often the deciding factor determining the formation of stones in predisposed persons. Where a hot climate is also damp, there is usually relative freedom from stone.

The author has investigated the colloid activity of the urine of certain racial groups and reaches some interesting

conclusions. Negroes are less liable to stone formation than the white races, and there appears to be greater urinary colloid activity in the former. In patients with renal calculi the urinary colloid content is decreased, but the colloid activity is raised in pregnancy, which may account for the fact that calculus formation is uncommon in pregnancy in spite of dilatation and stasis in the urinary tract. Finally, the author found that the injection of hyaluronidase increased colloid activity in 82% of subjects, the greatest response being in the negro and the least in subjects harbouring calculi. Urine specimens from patients who had received hyaluronidase remained free of sediment for a longer period than urine from the same subjects taken before hyaluronidase was given. *Roland N. Jones*

1244. **Urinary Colloids in the Prevention of Kidney-stone Formation**

A. J. BUTT and E. A. HAUSER. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 604–607, April 17, 1952. 5 figs., 1 ref.

The chemical reactions which result in the formation of urinary calculi have been the subject of much research, but are still far from clear. The urine contains salts, both electrolytic and non-electrolytic, which remain dissolved in much higher concentration than their solubility in water would permit, the presence of colloids in the urine preventing their precipitation from these supersaturated solutions. But since the mechanism of this colloid–crystalloid reaction is not fully understood, it is impossible for the clinician to define with certainty the conditions in which stones will form.

It has been shown that there is a higher concentration of colloids in the urine of negroes than of whites, of women than of men, and of pregnant women than of non-pregnant women; and in each case, the former is less subject to stone formation.

As urine of high surface tension is associated with a history of stone formation, it is suggested that it is the capillary-active colloids, with their dispersive and emulsifying properties, which are active in the prevention of stone formation. Certain substances, as, for example, hyaluronidase, possess these properties to a high degree, and their excretion or destruction in the urine may be important factors in the production of urinary lithiasis. Similarly their administration may be valuable in the treatment and prophylaxis of stone. *James Kemble*

MALE GENITALIA

1245. **Carcinoma of the Prostatic Bed after Prostatectomy.** (La cancérisation de la loge prostatique après prostatectomie)

E. CHAUVIN. *Journal d'Urologie Médicale et Chirurgicale* [*J. Urol. méd. chir.*] **57**, 772–783, 1951. 4 figs. [Received May, 1952]

The obstruction caused by the involvement of the prostatic bed by carcinoma following prostatectomy has not been so fully described as that due to scar tissue. Neoplasm involving the prostatic bed may be due to: (1) malignant changes in an adenomatous prostate which had not been detected before enucleation; (2) carcinoma starting initially in the remains of the prostatic tissue left after enucleation; (3) an epithelioma starting in the scar tissue resulting from prostatectomy. The first group is the most common, and symptoms of malignant involvement tend to occur within a few months; the second group is of less frequent occurrence, the symptoms of carcinoma arising only after a few years of apparently good health.

The indications which should arouse suspicions in the early stages are: a difficult enucleation, with a tendency to excessive postoperative bleeding, a prolonged, stormy convalescence, and a delay in the healing of the suprapubic wound. The urine frequently remains infected or becomes so, and has a particularly foetid odour. Dysuria with marked scalding is characteristic, but is to be differentiated from the retropubic pain which may also occur but which is unrelated to the fullness of the bladder and tends to radiate into the loins and legs. Haematuria may be obscured by the pyuria or it may be the predominant feature. Nocturnal frequency is more marked than in the case of an enlarged benign prostate. Progressive urinary obstruction is the most characteristic feature, the patient having the sensation of passing urine against a rigid blockage, which differs from that of the more yielding obstruction of the adenomatous prostate. Catheterization reveals a narrowing of the prostatic urethra (which may admit only a 15 F sound) and some residual urine. Rectal palpation usually reveals a large mass adherent to the symphysis pubis, indurated, and irregular in outline and consistency, or there may be two or three hard, painless, but discrete nodules; in other cases only part of the prostatic bed may be involved. A urethrogram often shows a marked elongated narrowing of the prostatic urethra or the presence of a cavity with irregular walls in the course of the urethra. When cystoscopy has been necessary in order to locate the source of haematuria it is not uncommon to find an irregular, nodular, or ulcerating tumour involving the trigone. Radiography of the skeleton may reveal metastases in the bones. The only conclusive method of diagnosis is by the removal of an adequate piece of tissue for microscopy.

The surest way of avoiding subsequent malignant change of the first type is by never performing enucleation in cases of benign adenomatous prostate if there is the least suspicion of carcinoma; in these cases hormone therapy or resection, or even cystotomy, should be preferred. In the second type only extensive removal of any remaining gland tissue after prostatectomy has been performed can lessen the incidence of carcinoma. Once this condition has been diagnosed, the first two types should respond to hormone therapy, while all three types may respond to deep *x*-ray therapy.

J. E. Semple

1246. **Rise of Serum-acid-phosphatase Level following Palpation of the Prostate**

O. DANIEL and J. J. VAN ZYL. *Lancet* [*Lancet*] **1**, 998–999, May 17, 1952. 1 fig., 3 refs.

Endocrinology

PITUITARY GLAND

1247. **Salicylates and Neuro-endocrine Stimulation**
H. VAN CAUWENBERGE and H. BETZE. *Lancet* [*Lancet*] **1**, 1083–1086, May 31, 1952. 9 figs., 14 refs.

By experiments at the University of Liège, in which male albino rats weighing 150 to 200 g. were used, the authors found that the circulating eosinophils and the adrenal ascorbic acid and cholesterol concentrations may be significantly depleted by an intraperitoneal injection of isotonic sodium salicylate (200 to 300 mg. per kg. body weight), the magnitude of the effect depending on the plasma salicylate level. A low blood salicylate level (6 to 7 mg. per 100 ml.) would still cause nuclear pyknosis in lymphoid tissue. All these effects were less pronounced in rats anaesthetized with allobarbitone.

The inhibition of the pituitary–adrenal mechanism by barbiturates, which, the authors suggest, takes place in the hypothalamus, would seem to be of importance in the treatment of certain endocrine disorders; the inadvisability of concurrent administration of barbiturates and salicylates in rheumatic disease is also suggested.

Norval Taylor

1248. **Alteration of Experimental Poliomyelitis Infection in the Syrian Hamster with the Aid of Cortisone**
G. SHWARTZMAN and A. FISHER. *Journal of Experimental Medicine* [*J. exp. Med.*] **95**, 347–362, April 1, 1952. 31 refs.

1249. **Treatment of Hypopituitary Coma**
H. L. SHEEHAN and V. K. SUMMERS. *British Medical Journal* [*Brit. med. J.*] **1**, 1214–1215, June 7, 1952. 1 ref.

A particular type of coma may occur in patients who have had hypopituitarism for several years. It sometimes follows a minor infection or an operation. The patient becomes gradually stuporous and then passes into deep coma. In some cases the hypoglycaemia is more severe than is usual in hypopituitarism, in some the blood levels of sodium and chloride are low, and in yet others hypothermia and bradycardia are pronounced. Death may occur during the coma or the patient may recover spontaneously after a few days.

The authors describe 9 cases in which the severe hypopituitarism was due to post-partum necrosis of the anterior lobe. Of the 9 patients, 2 died and 2 who were not deeply comatose recovered spontaneously with rest in a warmed bed. A fifth patient who had a temperature of 87° F. (30·5° C.), no pulse at the wrist, and a heart rate of 41 per minute recovered in 90 minutes when he was immersed in a bath of water the temperature of which was gradually increased; the same treatment was repeated successfully with the same patient on a later occasion. Intravenous glucose was given in 4 cases, with beneficial effect in 2. Cortisone (in doses of 125 mg. intravenously at half-hour intervals for 90 to 180 minutes) and deoxycortone acetate were without effect.

H. Herxheimer

1250. **Hypopituitarism with Pituitary Tumours. Cortisone in the Treatment of Stupor Associated with Hypopituitarism**
J. E. CAUGHEY, A. JAMES, and E. K. MACLEOD. *British Medical Journal* [*Brit. med. J.*] **1**, 1216–1219, June 7, 1952. 11 refs.

In 3 cases of chromophobe adenoma of the pituitary gland and one of craniopharyngioma the tumour was removed at operation. In all the patients there were clinical signs of hypopituitarism which was confirmed by insulin sensitivity tests and estimation of the urinary excretion of 17-ketosteroids. Immediately after operation the patients passed into a semicomatose state in which the pulse could be felt, the superficial and deep reflexes were present, but there was marked confusion, disorientation, and incontinence. Amnesia continued for the period of stupor. One of the 4 patients gradually recovered within 6 weeks without treatment. Another patient, after having been semicomatose for 2 weeks, received an implant of 200 mg. of testosterone and 100 mg. of deoxycortone acetate, together with daily doses of sodium chloride and thyroid; he started to improve markedly 6 days later and made a good recovery. The 2 remaining patients, who were given 200 mg. of cortisone daily when the stupor started, responded after 28 and 48 hours respectively; cortisone was later replaced by testosterone, deoxycortone acetate, and thyroid.

H. Herxheimer

1251. **A.C.T.H. in Hypopituitarism**
C. F. ROLLAND and J. D. MATTHEWS. *British Medical Journal* [*Brit. med. J.*] **1**, 1220–1222, June 7, 1952. 2 figs., 7 refs.

The authors describe 3 cases of hypopituitarism in which the basal metabolic rate was low and the excretion of 17-ketosteroids was reduced; 3 further cases are mentioned briefly in an addendum. The patients received 50 to 75 mg. of corticotrophin daily over a period of 10 days. A marked subjective improvement became apparent on the third day of treatment and persisted until about 3 days after treatment stopped, when a relapse began. Testosterone and thyroid were then substituted [but the effect of this treatment is not reported]. The subjective improvement was accompanied by objective signs of improvement—a decrease in insulin sensitivity and an increase in capillary resistance in one patient and an increase in urinary excretion of 17-ketosteroids or of corticoids in the other 2 patients.

H. Herxheimer

1252. **The Anaemia of Hypopituitarism**
V. K. SUMMERS. *British Medical Journal* [*Brit. med. J.*] **1**, 787–790, April 12, 1952. 26 refs.

Hypopituitarism is now believed to be due in the great majority of cases to post-partum necrosis of the anterior lobe of the pituitary body. A normochromic anaemia of moderate severity and refractory to treatment is usual in this condition, but examples of both hypochromic and hyperchromic anaemia have also been reported. Accurate classification of the anaemia seems to be impossible.

The author studied the haematological changes in 10 patients, all but one of whom had typical hypopituitarism due to post-partum necrosis of the anterior lobe, with amenorrhoea since their last delivery, absent pubic and axillary hair, cold-sensitivity, reduced basal metabolic rate and 17-ketosteroid excretion, and with a typical response to the insulin-sensitivity test. Blood was obtained by venepuncture from an antecubital vein and placed in a 5-ml. bottle containing Wintrobe's anticoagulant mixture. To prevent deterioration 1 ml. of 40% formalin was added to this mixture. Subsequently erythrocyte and reticulocyte counts were made, haematocrit values determined, and the haemoglobin content measured by means of a photo-electric absorptiometer. The methods available for determination of erythrocyte diameter are open to many inaccuracies and for this reason no direct measurement was made. The usual gruel meal was used for assessing gastric acidity.

In 6 cases the anaemia was macrocytic and hyperchromic. Clinically 3 of these patients had marked, and 3 moderate, myxoedematous features. Histamine-fast achlorhydria was present in all the cases in which the test was performed. The bone marrow was normoblastic in all cases. In the remaining 4 cases the anaemia was normocytic and hypochromic. Atrophy of the mucous membrane of the tongue with perlèche was observed in only one of the 10 cases, in which the anaemia was of normocytic type. There are no reports in the literature of either perlèche or koilonychia occurring in cases of hypopituitarism associated with anaemia. Various methods of treatment were tried in these cases, including thyroid, testosterone, iron, liver, cortisone, and corticotrophin. The response to thyroid, testosterone, liver, and iron was unsatisfactory, but cortisone and corticotrophin produced a prompt increase in the erythrocyte count and the haemoglobin concentration.

A. Forbath

1253. **The Course of Anterior Hypopituitarism**
D. HUBBLE. *Lancet* [*Lancet*] **1**, 1123–1131, June 7, 1952. 12 figs., 44 refs.

A general survey is presented of the various types and causes of hypopituitarism, with brief case reports and a review of the literature.

A developmental defect may lead to gonadotrophin deficiency. Hypopituitarism is reported in 2 male first cousins, one a dwarf and the other showing eunuchoid characteristics. The evidence for a form of hypopituitarism due to poor nutrition is reviewed; 2 cases due to adult coeliac disease, in neither of which was there urinary excretion of gonadotrophin, are described. Psychogenic factors may lead to anorexia nervosa, and a study of hormone production in this condition indicates a considerable degree of associated hypopituitarism. The amenorrhoea may precede the anorexia, and the gonadotrophin deficiency may result from either the psychogenic or the nutritional cause, or from both. The case is described of a boy of 9 years who was considered to have anorexia nervosa comparable to the adult form of the disease.

Destructive lesions, such as the post-partum necrosis of the anterior lobe described by Sheehan, account for a large group of cases. In a man in whom the anterior lobe of the pituitary had been almost completely destroyed, the cause of which was uncertain, death ultimately resulted from pneumonia. At necropsy the endocrine glands were atrophic, and the only recognizable layer remaining in the adrenal cortex was the zona glomerulosa. In such cases gonadotrophin function fails first, thyrotrophic and adrenotrophic function only very much later. As a result myxoedema is not likely to be due to hypopituitarism in the absence of sexual failure.

Evidence of hypopituitarism was found in a case of haemochromatosis. Urinary excretion of 17-ketosteroids and gonadotrophin output were both low, but there was no hypothyroidism or disturbance of water excretion. At necropsy iron was deposited in the basophil cells of the pituitary; the zona fasciculata of the adrenal cortex was well preserved, but the reticularis had almost disappeared.

The experimental and clinical findings indicate that in depression of the anterior lobe of the pituitary from any cause, sex hormones are early and always involved. Thyroid and adrenocortical hormones are disturbed much less easily. Functions of homeostasis take precedence over the less essential functions of reproduction and growth.

C. L. Cope

THYROID GLAND

1254. **Carcinoma of the Thyroid and Non-toxic Nodular Goiter**
E. J. CERISE, S. RANDALL, and A. OCHSNER. *Surgery* [*Surgery*] **31**, 552–561, April, 1952. 23 refs.

There were 51 cases of carcinoma of the thyroid among 580 cases of nodular goitre seen at the Ochsner Clinic, New Orleans, during 1942–9. In 387 cases there was a single nodule, and the incidence of carcinoma was higher in this group than in the cases of multiple nodular goitre. The sex ratio in the cases of carcinoma was 3 women to 1 man (in the cases of non-toxic goitre it was 5 to 1), and the mass had been present for an average of more than 5 years.

Early diagnosis of carcinoma of the thyroid by clinical means is not yet possible and the authors therefore favour thyroidectomy in all cases of nodular goitre. Radical neck dissection and hemithyroidectomy is advised in all cases of enlarged lymph nodes, invasion of neck muscles, or nerve palsy. Even where complete local resection is impossible, decompression of the trachea should be

carried out with removal of as much of the tumour as possible.

The authors found that the 5-year survival rate was similar to that reported by other workers, namely, nearly 80% in cases of papillary adenocarcinoma, only 25% in cases of follicular and alveolar carcinoma, and *nil* in cases of giant- or spindle-cell carcinoma. They also agree that " lateral aberrant thyroid " represents metastasis from a primary carcinoma of the thyroid.

Guy Blackburn

1255. **The Status of Lymphadenoid Goitre, Hashimoto's and Riedel's Diseases**
T. LEVITT. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **10**, 369–404, June, 1952. 12 figs., 40 refs.

1256. **Uptake in Treated Hyperthyroidism**
F. K. BAUER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **223**, 495–501, May, 1952. 5 figs., 9 refs.

The increased sensitivity of gamma-ray detectors now makes it possible to estimate thyroid activity with very small doses of radioactive iodine (^{131}I), thus permitting more frequent assays without hazard to the patient. The author reports his observations on the uptake of ^{131}I in 60 thyrotoxic patients before and after treatment by thyroidectomy, and with Lugol's solution, thiouracil, and ^{131}I. The investigation was made at the Radioisotope Unit, Veterans Administration Center, Los Angeles. The patients were given 1 or 2 μc. of ^{131}I either intravenously or orally and the thyroid uptake was estimated at 30 minutes and 1, 3, 6, 24, and 48 hours after administration. Results from 88 readings on normal subjects were first recorded in order to obtain the normal range, and then 60 thyrotoxic patients in varying stages of thyroid activity were investigated.

It was shown that in the normal subject 62% of the 24-hour uptake occurred in the first 6 hours, whereas in the thyrotoxic patient this figure was over 66%, although the total was naturally much greater. Also, although the maximum uptake of ^{131}I returned to normal after suitable therapy, the speed of uptake was unaltered, that is, more than two-thirds of the 24-hour uptake still occurred in the first 6 hours. This was also true following thyroidectomy, and it is therefore assumed that the residual gland after thyroidectomy retains its avidity for ^{131}I; it is also assumed, with experimental backing, that after ^{131}I therapy there remain islands of hyperactive thyroid tissue which continue to accept the isotope with alacrity. It is not so clear why this rapid uptake continues after treatment with Lugol's iodine and thiouracil (the author was unable to observe the effect after deep *x*-ray therapy). He concludes that treatment results in a quantitative rather than a qualitative change in the thyrotoxic gland.

In certain cases of suspected thyrotoxicosis the standard investigations have given negative results, but the same high rate of uptake has been found: these are being studied to determine whether this sign is a pre-toxic phenomenon. *J. N. Harris-Jones*

1257. **A Plasma I^{131} Index for Assessing Thyroid Activity**
H. BLONDAL. *British Journal of Radiology* [*Brit. J. Radiol.*] **25**, 260–262, May, 1952. 1 fig., 10 refs.

The author suggests a simple method of assessing thyroid toxicity by total plasma estimations of radioactive iodine (^{131}I). The plasma radioactivity in normal and hyperthyroid states was studied after the administration of an oral tracer dose of ^{131}I (50 to 100 μc.). In the normal subject the value was high in the first few hours after administration of ^{131}I, and low after 2 days had elapsed. This relationship was reversed in thyrotoxicosis. This difference is clearly demonstrated by comparing the ratios obtained when the 48-hour value is divided by the 2-hour value.

The 48-hour:2-hour ratios were studied in 4 thyrotoxic and 7 euthyroid patients. In the thyrotoxic subjects the 48-hour:2-hour ratio ranged from 1·75 to 2·75, and in the euthyroid group from 0·05 to 0·26. The separation between the normal and toxic series was better (by a factor of about 2) using the 48-hour:2-hour index than with the other methods used, namely, thyroid uptake, plasma clearance rate, and urinary excretion of iodine.

Edward M. McGirr

PARATHYROID GLANDS

1258. **Mental Changes Associated with Hyperparathyroidism. Report of Two Cases**
T. E. FITZ and B. L. HALLMAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **89**, 547–551, April, 1952. 1 fig., 11 refs.

The term " parathyrotoxicosis " has been used to describe the condition in which blood calcium levels are extremely high. The most bizarre clinical pictures may be presented and sudden death may occur. Sometimes the primary manifestations are psychic. The cause may lie in the increased electrical resistance of the nerves in these cases or in the metastatic calcium particles sometimes found in the brain tissue. Two cases showing severe mental changes are described.

In the first of these cases the patient complained of colicky lower abdominal pain associated with disturbance of micturition, pain in the chest on exertion, and occipital headache. Overshadowing these multiple complaints was the paranoid personality of the patient, manifested in repeated references to " evil influences ", " his lack of wealth, which made people plot against him ", " voices ", and " heavenly music ". Removal of a parathyroid adenoma resulted in a remarkable clearing of the mental condition associated with a fall in the blood calcium level from 14 to 10 mg. per 100 ml. Although the patient remembered the feelings of persecution 2 weeks after the operation, he was able to mix with patients in the ward and showed no mental confusion.

The second patient began to tire easily and suffer from nervousness, insomnia, and loss of memory. Serious personality changes followed. He became confused and irritable and his manner varied from great depression to great elation. He drank heavily, used obscene language, and became unmanageable. The blood calcium level

was 19 mg. per 100 ml. Uraemia was suspected because of hypertension and an elevated non-protein nitrogen level. Following operation for removal of a parathyroid adenoma the serum calcium level returned to normal and in the opinion of his family he was his normal self 24 hours after the operation.

[The rapidity of the change in the mental state argues against this syndrome being due to " particles of metastatic calcium in the brain ". The cause may lie in the parathyroid hormone or in the raised calcium level in the blood. Mental changes may follow hypervitaminosis D.]

Robert Hodgkinson

ADRENAL GLANDS

1259. **Further Observations on Capillary Resistance and Adrenocortical Activity**

H. N. Robson and J. J. R. Duthie. *British Medical Journal* [*Brit. med. J.*] **1**, 994–997, May 10, 1952. 6 figs., 7 refs.

In each of 6 cases of hypopituitarism capillary resistance, as measured by the negative-pressure method described by the authors (*Brit. med. J.*, 1950, **2**, 971), was abnormally low. The intramuscular injection of 50 mg. of corticotrophin daily was followed by a rise in capillary resistance and dramatic clinical improvement. After the injections were stopped there was a prompt clinical relapse with an abrupt fall in capillary resistance. The response was more easily invoked by adrenaline or insulin; an injection of 0·6 mg. of adrenaline subcutaneously or of 4 units of insulin intravenously led to a rise in capillary resistance, whereas a single dose of 25 mg. of corticotrophin was without effect.

Cortisone was given to 15 patients, 9 of whom were suffering from rheumatoid arthritis. In 11 patients intramuscular injection of 100 mg. daily was followed by a response similar to that induced by 50 mg. of corticotrophin daily, though the response developed more slowly. In 3 patients who responded clinically to cortisone by mouth a rise in capillary resistance occurred within 6 hours of a dose of 50 mg.; in a fourth case there was neither clinical response nor change in capillary resistance.

The rise in capillary resistance appeared to be a sensitive index of adrenal cortical response, occasionally more sensitive than the fall in the eosinophil count.

In contrast, injection of deoxycortone acetate in doses of 10 to 30 mg. in 2 patients was followed by a fall in capillary resistance, which was maximal about 12 to 16 hours after the injection. Administration of progesterone, testosterone, oestradiol benzoate, or pregnenolone was without effect.

The authors conclude that the rise in capillary resistance previously demonstrated after various stresses may be due to increased production of glucocorticoids by the adrenal cortex. They suggest that if changes in the skin capillaries are representative of changes throughout the capillary bed, these findings may throw light upon the mode of action of cortisone in inflammatory conditions and other disease states. *Robert de Mowbray*

1260. **Adrenal Cortical Function at Death as Measured by Level of Circulating Eosinophils**

P. B. Jennings. *British Medical Journal* [*Brit. med. J.*] **1**, 1055–1058, May 17, 1952. 4 figs., 28 refs.

It is now generally accepted that the adrenal cortex is concerned in adapting to stress, whether internal or external, but no observations have previously been made on the activity of the cortex if the stress persists until the organism dies. In the present paper, from Atlanta, Georgia, the findings in 62 moribund patients are described, the object of the investigation being to help clarify the functional status of the adrenal cortex during the final phase of exhaustion and at death.

Adrenal cortical function was assayed by estimating the level of circulating eosinophils. Counts were made daily up to the time of death or until the patient was obviously recovering. Of the 62 patients, 12 survived. For purposes of control 54 subjects were taken at random from a wide range of healthy individuals and non-moribund hospital patients, some of the latter being acutely ill.

Of the control group only 10% had fewer than 30 eosinophils per c.mm. (taken as the lower limit of normal in this study), and in fact a few of the control subjects were suffering from conditions known to cause a temporary eosinopenia. In the moribund group 94% of those who died had fewer than 30 eosinophils per c.mm. on the day of death, and in half of these the count was *nil*. In the 12 patients who survived there was an initial eosinopenia, but the count was normal by the time they had recovered enough to sit in a wheel-chair.

These results show that, if the level of circulating eosinophils is a reliable index of cortical activity, there is no failure of the adrenal cortex during the terminal stages of illness; on the contrary, there is hyperactivity until the moment of death. Treatment with cortisone is not therefore indicated in the moribund patient unless the drug is specific for the disease. *Nancy Gough*

1261. **Effect of Repeated Injections of A.C.T.H. upon the Bone Marrow**

G. Hudson, G. Herdan, and J. M. Yoffey. *British Medical Journal* [*Brit. med. J.*] **1**, 999–1002, May 10, 1952. 10 refs.

The effect of repeated injections of corticotrophin on the bone marrow of guinea-pigs of the Mill Hill strain, 4 to 6 months old, was studied. In 7 normal guinea-pigs blood from an ear vein was taken for a blood count, the guinea-pigs then being killed and the bone marrow examined. To 9 other guinea-pigs, after a blood count, daily intraperitoneal injections of 1 mg. of corticotrophin were given for 7 days. The corticotrophin was dissolved in 0·3 ml. of physiological saline containing 0·001/N HCl. At the end of the course of injections another blood count was made, the animals were killed, and the marrow was examined.

Absolute and differential blood counts were made with Wright's stain and water at *p*H 6. The eosinophils were counted by a modification of Randolph's technique, a mixture of equal parts of propylene glycol and 0·05% phloxine in water being used as the diluent. Reticulo-

cytes were counted by the brilliant cresyl-blue method—1% in absolute alcohol allowed to dry on the slide. Marrow from the humerus was ejected into a known weight of human plasma in a tube and the weight of marrow obtained by difference. The tube was shaken 400 times per minute for 3 minutes in a mechanical shaker to suspend the cells. Marrow smears and eosinophils were stained by the methods indicated above.

The marrow as a whole appeared to show increased cellularity in the corticotrophin-treated animals and there was an increase in the number of myeloid cells. There were no significant changes in the marrow lymphocytes. The relationship of corticotrophin to the bone marrow is discussed. *Norval Taylor*

1262. **Isolation of a Highly Active Mineralocorticoid from Beef Adrenal Extract**
H. M. GRUNDY, S. A. SIMPSON, and J. F. TAIT. *Nature* [*Nature, Lond.*] **169**, 795–796, May 10, 1952. 1 fig., 7 refs.

1263. **Secretion of a Salt-retaining Hormone by the Mammalian Adrenal Cortex**
S. A. SIMPSON, J. F. TAIT, and I. E. BUSH. *Lancet* [*Lancet*] **2**, 226–228, Aug. 2, 1952. 8 refs.

DIABETES MELLITUS

1264. **Skeletal Changes in Diabetes Mellitus in Adults.** (Skelettveränderungen bei Diabetes mellitus der Erwachsenen)
C. A. HERNBERG. *Acta Medica Scandinavica* [*Acta med. scand.*] **143**, 1–14, May 10, 1952. 4 figs., 4 refs.

Material from necropsies on 10 female and 4 male diabetics between the ages of 33 and 75 years were examined at the Cantonal Hospital, St. Gallen, Switzerland. Thin macerated slices of vertebral bodies, iliac bone, ribs, head of femur, distal part of radius, and skull were investigated for porosity and bone structure. Radiological and histological examination showed in all cases a condition of "osteoblastic osteoporosis". Osteoclastic activity was usually normal, but osteoblastic activity was reduced; there was an over-all reduction of bone substance, and bony trabeculae were smooth and small. The Haversian canals were often dilated. Osteoclasts and Howship's lacunae were usually normal, and there was rarely fibrosis of marrow spaces. Only in severe osteoporosis were skeletal deformities met with.

Three degress of osteoporosis were distinguished on macroscopical and microscopical grounds, ranging from Grade 1, where reduction of bone was confined to the centre, to Grade 3, where even the cortex was porous. In order to assess whether the changes were merely due to age, bones from 14 other normal cases of similar age and sex were used as controls. No significant differences were observed, except in the younger groups, where osteoporosis was markedly greater in diabetics. In older patients the degree of osteoporosis was related also to the duration of the diabetes, although it was present in some degree in those who had had diabetes for only a short time. The osteoporosis was generally evenly distributed throughout the skeleton, but in one case the spine was more severely affected, leading to osteophyte formation in the lower ribs and at the iliac crests because of approximation. These findings are similar to those in Cushing's syndrome. Osteoporosis in diabetes is another pre-senile change like arteriosclerosis. *E. Neumark*

1265. **Two Cases of Diabetes Mellitus in Infants under 1 Year**
H. S. BRODRIBB, J. MCMURRAY, and L. G. SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 1060–1061, May 17, 1952. 3 refs.

1266. **Diabetes Mellitus and Vascular Disease.** (Diabete mellito e patologia vasale)
G. C. DOGLIOTTI, G. LENTI, and C. MATTEI. *Minerva Medica* [*Minerva med., Torino*] **1**, 2–8, Jan. 5, 1952. 11 figs., 39 refs.

At Turin University the cardiovascular system of a large number of diabetic patients was investigated by means of pulse tracings, electrocardiograms, retinal examinations, and capillary microscopy. Diseased states of the cardiovascular system were present in about 75% of the patients, and treatment had little influence on the course of these disturbances. Most of the patients had a raised blood cholesterol level. The incidence of vascular disease increased with the duration of diabetes; renal disease of vascular origin, particularly hypertension, was common, but Kimmelstiel and Wilson's intercapillary glomerulosclerosis was rare. These observations apply almost equally to diabetics of all ages. In diabetes it is the smaller vessel which is most frequently affected, and manifestations of vascular disease are usually widespread. *E. Neumark*

1267. **The Capillaries and the Process of Coagulation of the Blood in Diabetes.** (Capillari e processo di coagulazione nel diabete)
C. MATTEI and G. CROLLE. *Minerva Medica* [*Minerva med., Torino*] **1**, 9–16, Jan. 5, 1952. 13 figs., 19 refs.

The authors investigated the bleeding time, clotting time, capillary fragility, prothrombin level, prothrombin consumption, platelet count, and clot retraction time in a series of 117 diabetic patients. The bleeding time was prolonged in only 2 patients and clotting time in only 9. Hess's capillary fragility test was positive in 22 patients, of whom 18 were more than 50 years old. The platelet count and prothrombin level were normal in most patients. The frequency of a positive capillary test in diabetes is stressed. *E. Neumark*

1268. **The "Plethoric" Form of Diabetes Mellitus.** (Sulla "forma pletorica" del diabete mellito)
G. LENTI and L. BRIGHENTI. *Minerva Medica* [*Minerva med., Torino*] **1**, 16–29, Jan. 5, 1952. 22 figs., 23 refs.

Among the diabetic patients (see Abstracts 1266–1267) observed at Turin University Clinic the authors' attention was drawn to a group of 14 who were obese and had erythrocytosis, a raised blood cholesterol level,

hypertension, and extensive advanced vascular and capillary lesions. The 11 men and 3 women were between the ages of 45 and 68 years, were heavy eaters, and generally of the "hyperpituitary and hyperadrenal type". The heart was usually enlarged, as was also the radiographic shadow of the aorta, and myocardial damage was often evident in the electrocardiogram. Blood volume, haemoglobin concentration, and the numbers of erythrocytes and platelets were increased in most cases. From the point of view of pathogenesis a relationship between this peculiar form of diabetes and Cushing's syndrome is suggested. Prognosis is usually rather poorer in these cases, particularly in view of the condition of the cardiovascular system, but a careful diet with reduction in carbohydrates and fats is often beneficial. *E. Neumark*

1269. **A Postmortem Study of Vascular Disease in Diabetics**
E. T. BELL. *Archives of Pathology* [*Arch. Path., Chicago*] **53**, 444–455, May, 1952. 12 refs.

This report is based upon a study of 1,559 autopsies made on diabetic subjects. In about 5% of the group diabetes developed before the age of 20 years; in 16% before the age of 40 years, and in 70% after the age of 50 years. There were no deaths from vascular disease before the age of 20 years. Between the ages of 20 and 40 years about 23% of the deaths were due to vascular disease. About 54% of the patients over 50 years of age died of vascular lesions. About 30% of non-diabetics over 40 years of age die of some form of vascular disease. Therefore, only about 24%, and not 54%, of the deaths of the older diabetics should be attributed to the diabetic state.

The types of vascular disease especially accelerated by diabetes are gangrene, renal arteriosclerosis, and coronary disease. When the onset of the diabetes is before the age of 40 years, the influence of the duration of the disease on the development of vascular lesions is striking. Few persons present vascular lesions during the first 10 years of diabetes; after 20 years or more of the disease only few escape Diabetes of long duration does not invariably terminate in a vascular death. In the older diabetics there appears to be no relation between the severity of the diabetes and the tendency toward vascular disease.

In this series the absence of vascular disease in a few long-term survivors may not be attributed to better control of the diabetes.—[Author's summary.]

1270. **Treatment of Diabetic Ketosis**
J. D. N. NABARRO, A. G. SPENCER, and J. M. STOWERS. *Lancet* [*Lancet*] **1**, 983–989, May 17, 1952. 8 figs., bibliography.

The results of extensive metabolic studies in some 70 cases of diabetic ketosis are applied in this article to the treatment of this condition. One death is reported in this series. The severe loss of extracellular water, sodium, and chloride, and the cellular loss of water, potassium, phosphate, and magnesium is confirmed. Therapy, therefore, to be effective must supply these electrolytes as well as insulin and water. The authors advocate early and large doses of insulin (about one-fifth of which should be given intravenously) repeated 2-hourly, with control by blood sugar estimations where possible. Alkali therapy is not advised, because of the possibility of alkalosis and excessive sodium administration. The authors' studies show that sodium and chloride are taken up in the ratio of 1·3:1, and that this need is best supplied by a solution of sodium chloride and lactate. Intravenous administration of fluids is usually necessary, 2 litres being commonly given in the first hour. Blood transfusion is considered to be the best means of combating shock.

The continuing controversy concerning early glucose administration is reviewed, but the authors advise against it on the grounds that it encourages osmotic diuresis and intensifies hypokalaemia. Its value when the blood sugar level begins to fall is not disputed. The uptake of potassium in the recovery period is shown graphically and the special need for its replacement is stressed, but administration should follow extracellular repair, when the potassium is passing back into the cells and the plasma level, initially high, is falling rapidly. This fall may, it is stated, be assumed to accompany a falling blood sugar level and therefore parenteral potassium therapy may be given without flame-photometry control. Replacement of phosphate and magnesium is also advised, and a solution incorporating these electrolytes is given. Oral administration of potassium and phosphate should continue in the recovery phase, together with a high-protein diet fortified with vitamin-B complex. A scheme of treatment for severe ketosis is given, and two illustrative case reports are included.

J. N. Harris-Jones

1271. **A Study of Ketonaemia in Diabetic Coma.** (Étude de la cétonémie dans le coma diabétique)
R. BOULIN, F. W. MEYER, M. GUÉNIOT, and C. LAPRESLE. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 1421–1425, May 6, 1952. 1 ref.

The level of ketone bodies in the blood was measured in 25 cases of severe diabetic ketosis and an attempt made to correlate the results with the clinical state. [Normal figures are not given and the methods of analysis are not stated.] The values ranged from 99 to 252 mg. per 100 ml., with a mean of 130 mg. There was no significant difference between the mean values for 9 conscious and 16 unconscious patients. The mean figure for dyspnoeic cases was only slightly higher (136 mg.) than for non-dyspnoeic cases (123 mg.). There was a tendency for higher ketone levels to be associated with higher blood glucose levels. There was no relation between the level of the alkali reserve on admission to hospital and the blood ketone level, nor between the latter and the time required to restore a normal alkali reserve. When the Gerhardt reaction in the urine became negative the blood ketone level was usually still above normal. The authors briefly mention a case in which the blood ketone level was 147 mg. per 100 ml. with a negative Gerhardt reaction in the urine.

C. L. Cope

The Rheumatic Diseases

1272. **A Contribution to Knowledge of the Relation between Chorea and Acute Rheumatism.** (Contributo alla conoscenza dei rapporti tra chorea minor e infezione reumatica)
A. POPPI. *Reumatismo* [*Reumatismo*] **4**, 242–252, May–June, 1952. 5 figs., 28 refs.

The author points out that although there is no specific test for the presence or absence of rheumatic infection, the antistreptolysin-O titre of the serum indicates quantitatively the degree of previous streptococcal infection. Thus if the titre were higher in cases of uncomplicated chorea than in normal subjects, this would be supporting evidence of a rheumatic basis. At the Rheumatism Centre of the University of Bologna three groups of children were examined. The groups each contained 55 children, similarly distributed as to age and sex, and consisted respectively of cases of " pure " chorea, cases of chorea with rheumatic manifestations, and cases of rheumatism without chorea. A titre of more than 400 units was taken to indicate previous infection with haemolytic streptococci, such titres being found in normal children in 6% of cases. In the group with pure chorea a titre of more than 400 units was found in 48%, in the group with chorea and rheumatism in 73%, and in the group with rheumatic fever in 70%, these figures being based on the mean of the last and first titres estimated in each case. The titres in cases of pure chorea never achieved the levels found in the other groups, but the author notes that the rise in titre in each case followed the same pattern in all 3 groups. There is therefore strong presumptive evidence that chorea is in some way related to rheumatism, although these observations do not provide any definite proof of the existence of such a relationship.

The author noted that the gain in weight during the course of an attack of pure chorea was far greater than in any other rheumatic episode, while others have pointed out that the blood pressure is higher in pure chorea than in other rheumatic diseases. He suggests, therefore, that in some subjects the response to streptococcal infection is limited to the nervous system, with stimulation of the pituitary gland, a higher production of corticotrophin, and a consequent reduction in the formation of collagen. *J. G. Jamieson*

1273. **A Follow-up Study of Tonsillectomy in Children with Rheumatism.** (Katamnestische Beurteilung der Tonsillektomie beim kindlichen Rheumatismus)
H. NETZSCH. *Münchener Medizinische Wochenschrift* [*Münch. med. Wschr.*] **94**, 971–975, May 9, 1952. 12 refs.

The author has attempted to assess the effects of tonsillectomy—so frequently suggested as a prophylactic measure on theoretical grounds—on the subsequent course of rheumatic fever (with and without endocarditis) and chorea minor by means of a 10-year follow-up study. Of the 319 patients studied, 80 had had their tonsils removed. On statistical analysis of the findings it was found that tonsillectomy appeared to reduce the incidence of recurrences of endocarditis and also to lessen the possibility of a fatal outcome, whereas it had no appreciable effect on the incidence of recurrence of joint symptoms. In chorea minor tonsillectomy would seem to be contraindicated, only 2 out of 15 patients subjected to tonsillectomy failing to relapse, compared with 41 out of 81 whose tonsils were not removed. A study of larger numbers is desirable. *D. Preiskel*

1274. **Creatine Metabolism in Arthritis**
J. E. DAWSON and H. B. SALT. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **11**, 23–29, March, 1952. 11 refs.

This paper is essentially a re-investigation of the work of Granirer (*Ann. intern. Med.*, 1949, **30**, 961) who claimed to show a significant increase in the 24-hour urinary creatine excretion in patients suffering from osteoarthritis. Using the improved technique of Peters (*J. biol. Chem.*, 1942, **146**, 179) the authors were unable to confirm Granirer's findings. Furthermore, of their 68 patients with rheumatoid arthritis or osteoarthritis 34 patients, 17 male and 17 female, showed no creatinuria. A slightly higher incidence and slightly greater degree of creatinuria did occur in the male rheumatoid group [but no criteria are given of the severity of the rheumatoid arthritis except the statement that all the patients were ambulant]. *R. E. Tunbridge*

1275. **The Natural History of Ankylosing Spondylitis.** (Sul nosografismo della spondilite anchilosante)
T. LUCHERINI and E. CECCHI. *Reumatismo* [*Reumatismo*] **4**, 125–153, March–April, 1952. 22 figs., bibliography.

The authors report their observations on 12 cases of ankylosing spondilitis seen at the Rheumatism Centre of the University of Rome during the year 1951. The patients' ages varied between 20 and 76, and only one was female. The cutaneous manifestations took the form of striae in the region of the knee (4 cases), where a rheumatic lesion was consistently demonstrated; in one case the striae appeared on the back, where they took the form of a herring-bone pattern radiating from the midline downwards and outwards; in 5 cases there was dilatation of the small cutaneous veins of the side of the chest wall, as has been reported a number of times by North American authors. One patient had a generalized psoriasiform eruption, and in this case the clinical picture deteriorated progressively. Evidence of focal sepsis was demonstrated in a number of cases and in one case there was active pulmonary tuberculosis, but there was not thought to be any relationship between the tuberculosis and the spondylitis,

except in so far as the former would tend to aggravate the latter. Arthritis was found in all cases of the series. It usually took the form of a polyarthritis of the ankles, shoulders, knees, hips, elbows, and wrists, decreasing in that order and relatively much less frequent in the metacarpal and metatarsal joints. In all cases there was sacro-iliac arthritis.

Radiological examination of the spinal column revealed in 4 cases a more or less typical " bamboo spine "; in 2 the syndesmosis affected the lower dorsal and upper lumbar regions, and in one the upper dorsal region only; in the fourth case there was no evidence of inter- or intra-vertebral ossification.

Iritis, which was found in one case, rapidly regressed with local cortisone therapy. The authors point out its importance, as it may be the first presenting symptom, and quote Teschendorff's dictum that all patients with iritis should have the spine examined radiologically. No cardiac changes were observed, and examination of the blood and urine revealed very little. Wasting was rather noticeable, there being muscular atrophy and loss of subcutaneous fat even though nutrition was adequate.

Splenectomy was performed in 3 cases in which there was definite enlargement of the spleen, but with little modification of the syndrome. The histological appearance revealed a non-specific chronic splenitis such as is found in rheumatoid arthritis, with fibrosis of the capsule, hyperplasia and collagenization of the splenic pulp, and sclerosis of the arterial walls. Biopsy of muscle showed a degeneration of muscle fibres, with small discrete collections of lymphocytes. No significant response was obtained from treatment with hyperpyrexia, gold salts, sex hormones, or salicylates. The only drug of any real value was cortisone. Radiotherapy even in the early stages was disappointing, confirming the results obtained by other [mostly British] workers.

The authors finally discuss the anatomical and pathological aspects of the disease and the various theories propounded by different authors. They conclude that ankylosing spondylitis is not an infective inflammatory process (though the initial stimulus may be of an infective nature), but is a particular proliferative process analogous in histological aspects to a special type of enchondroma of the intervertebral disk. In the present state of our knowledge it is their conviction that there is no valid argument against classifying ankylosing spondylitis as a vertebral variety of rheumatoid arthritis.

Edgar J. Gatt

RHEUMATOID ARTHRITIS

1276. **The Electromyogram in Rheumatoid Arthritis**
E. E. MUELLER and S. MEAD. *American Journal of Physical Medicine* [*Amer. J. phys. Med.*] **31**, 67–73, April, 1952. 4 figs., 16 refs.

The authors have investigated the electromyogram in 25 cases of rheumatoid arthritis at the Washington University School of Medicine, St. Louis, Missouri. Using this method of investigation they set out to assess the theory that muscle spasm is a cause of the muscle atrophy associated with the disease. The 25 patients, 9 male and 16 female, whose ages ranged from $4\frac{1}{2}$ to 73 years, had been suffering from rheumatoid arthritis for periods varying from 1 to 22 years. A group of 25 uncomplicated orthopaedic cases was taken as a control. The apparatus used [not described in detail] consisted of suitable amplifiers with photographic recording from cathode-ray oscilloscopes. The action potentials were detected by the use of both surface and co-axial needle electrodes.

It was found that no spontaneous activity could be detected with the subject at rest, provided that the position of the muscle tested was carefully adjusted. (Exceptions were found only in cases where concurrent neurological disorders existed.) The recordings during voluntary activity showed essentially a reduction in amplitude of the normal interference pattern, as is found in debilitating diseases; occasionally, isolated potentials of the myopathic type were observed. A few patients [number unstated] were examined before, during, and after treatment with cortisone and corticotrophin. No change in the action potentials was observed as a result of treatment with these drugs, except that it was found to be easier to position the patient to secure electrical inactivity of a muscle at rest during the course of the treatment.

The discussion is mainly concerned with the evaluation of theories regarding the cause of muscle weakness and atrophy in rheumatoid arthritis, and the authors consider that their results are compatible with the theory that the atrophy is due to a central inhibitory state in the spinal cord mediated by the pain impulses from the local lesions.

[The authors offer no positive evidence in support of this theory, but their results show that in their small series there was no evidence of disturbance of the normal mechanism of neuromuscular transmission in rheumatoid arthritis, and they were able to find no unequivocal evidence of muscle spasm in any of their cases.]

Kenneth Tyler

1277. **Familial Incidence of Rheumatoid Arthritis and Acute Rheumatism in 100 Rheumatoid Arthritics**
R. W. BARTER. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **11**, 39–46, March, 1952. 9 refs.

The familial incidence of rheumatoid arthritis and acute rheumatism in 100 patients suffering from rheumatoid arthritis and in 100 controls has been studied. The incidence of these diseases was 5·3% in the relatives of patients and only 2·4% in the relatives of controls; it was 11% and 4·6% respectively when brothers and sisters only were considered. Approximately two-thirds of all patients with rheumatoid arthritis gave a family history of this disease or of acute rheumatism. It is suggested that there is an heredo-familial tendency towards these diseases in some families, and that certain individuals may have a " hereditary weakness in their adaptation mechanism " together with a constitutional tendency to respond to the products of an antigen–antibody reaction through the medium of the synovial membrane.

Kathleen M. Lawther

1278. **The Effect of Cation-exchange Resins in Preventing Water Retention during the Treatment of Rheumatism with Cortisone.** (Azione antiedemigena delle resine a scambio di cationi nei reumatici sottoposti a cura cortisonica)

T. LUCHERINI and G. VENIALI. *Minerva Medica* [*Minerva med., Torino*] **43**, 821–822, April 19, 1952. 4 refs.

Disturbance of electrolyte balance is one of the undesirable side-effects of protracted treatment with cortisone, which leads to sodium chloride retention and potassium loss, thus producing oedema, increase in weight, and polydipsia, accompanied by hypochloraemic alkalosis, muscular weakness, and changes in the electrocardiogram. Treatment with mercurial diuretics, ammonium chloride, and low-chloride and high-potassium diet, has proved unsatisfactory.

Cation-exchange resins have been found effective in preventing water retention in hepatic cirrhosis, Cushing's syndrome, and nephrosis. These resins have a complex structure which enables them to take up one ion, such as potassium, in exchange for another, such as ammonium. The authors used a mixture containing 59% of a carbosilicate resin, 29% of its potassium salt, and 12% of a polyaminic-formaldehyde anion-exchange resin (" carboresin "). This mixture is reputed to prevent the danger of hypopotassaemia, and especially the unwelcome acidosis caused by the liberation of chlorides, the anion-exchange part of the mixture eliminating the danger of low alkaline reserve. The mixture was given orally in doses of 15 g. daily for 5 to 7 days, and repeated if necessary. In patients with concurrent prolonged cortisone treatment the same amount was given for 10 days, and then every 3 days during cortisone administration.

In oedematous patients this treatment produced an immediate and considerable increase of diuresis, with concomitant loss of weight. In patients who received the treatment from the beginning of cortisone therapy there was no disturbance of electrolyte metabolism and no sign of oedema. The dose of 15 g. daily is much lower than the 40 or 50 g. used in hepatic cirrhosis, but was usually sufficient, and was well tolerated by patients having a prolonged course of cortisone (up to 50 mg. daily). The blood potassium level was not significantly influenced. *V. C. Medvei*

1279. **Assessment of Rapidly Acting Agents in Rheumatoid Arthritis. Observations on Deoxycortone with Ascorbic Acid, A.C.T.H., and Cortisone**

G. E. LOXTON, D. LE VAY, and B. STANFORD. *Lancet* [*Lancet*] **1**, 1280–1285, June 28, 1952. 4 figs., 30 refs.

For assessing rapid changes in the rheumatoid state purely objective measurements of the state of the joints are unsatisfactory, as they are relatively insensitive, do not confirm clinical observations, and take no account of subjective changes. On the other hand, purely subjective factors cannot be measured precisely enough for test purposes. The authors therefore recommend that such assessments be based on objectively measurable factors which are affected by subjective changes, that is, certain components of joint function such as range and speed of movement, dexterity, and strength of grip. These factors must be such that accurate measurement can be made, and that some reasonable, even if arbitrary, standard of normality can be fixed. The function to be measured must also be impaired and capable of improvement, while skilled functions must be avoided in which normal standards change with practice. Joint-goniometry and grip-dynamometry are too inaccurate and insensitive to be of use in the measurement of functional changes. With these considerations in mind the authors have devised a technique for assessing the effect, in cases of rheumatoid arthritis, of certain rapidly acting drugs on the range of active joint movement and on joint " mobility " (that is, speed of movement). For this purpose an ingenious device is used whereby still and ciné photographs are taken as the patient performs certain movements, the range and speed of which can then be accurately measured. The results are expressed as percentages of arbitrary normal values derived from examination of the active range and mobility of a series of normal joints by the same technique.

In a series of measurements on 31 patients (70 joints) a statistically significant degree of improvement followed within an hour of the injection of 5 mg. of deoxycortone and 1 g. of ascorbic acid in 21 cases, but no significant change followed saline injections. The improvement was not usually maintained for longer than a week. In 3 out of 4 patients who were given 25 mg. of corticotrophin intravenously a well-marked improvement was observed within 1 hour, lasting up to 12 hours.

The authors consider that their findings confirm the original observations of Lewin and Wassén (*Lancet*, 1949, **2**, 993; *Abstracts of World Medicine*, 1950, **7**, 522) of the beneficial effects of deoxycortone and ascorbic acid in rheumatoid arthritis. To account for the conflict that has arisen over the merits of this therapy the authors stress the importance of time-relation between the injection and its effect—the average duration of the response is about 8 hours and may be only 30 minutes. In addition the response is inconstant, varies in magnitude, and may be followed by exacerbation. Reasons are given for believing that deoxycortone and ascorbic acid act in essentially the same way as does cortisone, but in an accelerated manner. *Ellis Dresner*

1280. **ACTH in the Treatment of Juvenile Rheumatoid Arthritis.** [In English]

J. VESTERDAL, O. REMVIG, and M. SPRECHLER. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **41**, 145–157, March, 1952. 4 figs., 9 refs.

A description is given of the treatment at the National Hospital, Copenhagen, of 7 children suffering from juvenile rheumatoid arthritis with daily doses of 24 i.u. of corticotrophin given for 6 to 14 days and then gradually reduced. A good effect was seen in most instances, but on cessation of treatment symptoms tended to recur. It is concluded that corticotrophin is indicated for the treatment of children who are developing deformities, or where deformities are present without osseous ankylosis.

D. P. Nicholson

Traumatic Surgery and Orthopaedics

1281. **Wounds and Internal Injuries Caused by Explosions.** (Organschäden und Körperverletzungen durch Druckstosswirkung von Explosionen)
W. SCHUBERT. *Virchows Archiv für Pathologische Anatomie und Physiologie* [*Virchows Arch.*] **321**, 295–325, 1952. 16 figs., 26 refs.

Research on the effects of explosions is only some forty years old. Little research was done in the first world war, and the first stimulus to extended research was provided by the civil war in Spain; this led to a series of British experiments which were continued into the second world war. According to the author similar experiments were not undertaken in Germany till 1943. In that year, arterial air embolism in victims close to the centre of an explosion was first described as a cause of death. In the same year the author described the earth-shock factor as an important component of injuries in explosions, and in 1944 he carried out experiments on the effects of gas-mixture explosions in closed chambers.

In 1914 Rusca showed that the pressure wave of an explosion acted directly on the thorax, compressing it and leading to the various haemorrhages encountered. In 1923 contusion pneumonia occurring some 8 days after the injury was described by Hanser. French and British research defined the zones of damage in the vicinity of explosions, but added little to the known causes of death. In 1947 Rössle described arterial air emboli more fully and showed that these occur in association with other injuries and particularly affect the coronary circulation. Investigation into the effects of earth shock were stimulated by the reports of calcaneal fractures in persons standing on solid floors in the neighbourhood of explosions. It was found that direct blows on the heel protected with a shoe, or even unprotected, did not produce fracture of the calcaneus, nor did the direct action of an explosion on the heel, and the explosion had to be intensified in effect by transmission through a solid surface to achieve any result.

Observation of bombing casualties led to the consideration of the effects of the earth-shock wave on the organs of individuals lying on the ground. Experiments on animals showed that this can produce thoracic and abdominal injuries; and a report on some troops who died as a result of bombing while lying in zig-zag trenches suggested that many of the changes found may be attributed to the earth shock as well as to the pressure wave. Experiments were then undertaken to separate the effects of a rise in gas pressure from those of the pressure wave, by investigating the explosion of gas mixtures in an elastic rubber container. This showed that the bronchi do not become dilated, and that the injuries which result are due to compression of the thorax which is forced into the position of complete expiration while at the same time the flanks are strongly compressed. As a result of this the pleurae are torn, the lungs compressed, and the pulmonary veins ruptured. In the abdomen the effects are determined in part by its gaseous contents. There are intestinal haemorrhages, peritoneal ruptures, and rupture of the liver. Damage tends to occur at the junction of the more solid with the more elastic parts of the body. Gross haemorrhages of the lungs are due to bleeding under increased pressure at the moment of shock. If the shock wave is not too short, blood is driven into the central organs; but primarily it is driven to the lungs, where there is a zone of diminished pressure due to the protection of the ribs. Air embolism is due to aspiration of air into the ruptured veins of the lung at the moment of decompression. Arterial air emboli are a special form of aspiration emboli from the lung. The primary cause of death is interruption of the circulation and damage to the heart. *J. G. Bonnin*

1282. **Intramedullary Nailing of the Ulna in Fractures of Both Bones of the Forearm in Adults**
C. E. ANDERSON. *Western Journal of Surgery, Obstetrics and Gynecology* [*West. J. Surg. Obstet. Gynec.*] **59**, 559–564, Nov., 1951. 5 figs., 3 refs.

A preliminary report is given of the results of treatment of 7 cases of fracture of both bones of the forearm in which intramedullary fixation of the ulna was carried out. An ordinary stainless-steel Steinmann pin was used. A variety of methods, including oblique screws and onlay bone-grafts, were employed in the treatment of the fractured radius. External cast fixation was maintained until radiographs showed solid bony union. The intramedullary nail was removed after union. The results in 6 of the 7 cases were satisfactory. *John Charnley*

1283. **A Disinfectant Barrier in Dressings Applied to Burns**
E. J. L. LOWBURY and A. M. HOOD. *Lancet* [*Lancet*] **1**, 899–901, May 3, 1952. 6 refs.

HAEMORRHAGE AND SHOCK

1284. **A Study of Oxypolygelatin in Human Subjects**
A. R. HIGGINS, H. A. HARPER, J. R. KIMMEL, T. W. BURNS, R. E. JONES, T. W. D. SMITH, and C. L. KLEIN. *Journal of Applied Physiology* [*J. appl. Physiol.*] **4**, 776–784, April, 1952. 5 figs., 20 refs.

Oxypolygelatin (OPG) is prepared from ossein or pigskin gelatin by condensation with glyoxal and subsequent oxidation with hydrogen peroxide. In 5% solution, which is the concentration used for intravenous administration as a "plasma volume expander" in the treatment of shock, it is liquid at room temperature and therefore compares favourably with gelatin, which tends

to gel at room temperature. The effect of the intravenous administration of 500 to 2,500 ml. of a 5% solution of OPG in physiological saline was studied at the U.S. Naval Hospital, Oakland, California, in 42 subjects, 7 of whom were in a state of shock and the remaining 35 healthy individuals. The time taken for the administration of each 500 ml. varied from 20 to 90 minutes. Six of the shocked patients " responded favourably " to this treatment.

The concentration of OPG in the plasma was highest at the end of the infusion and fell off rapidly for about 4 hours thereafter, the fall being subsequently much slower. Detectable amounts were still present in the plasma 48 hours after the infusion in 6 of the 8 cases observed for this length of time. The urinary excretion of OPG was rapid for about 3 hours after the infusion; after 8 hours about 50% of the dose administered had been excreted, 20% remained in the plasma, and the remainder could not be accounted for. OPG was found to increase the erythrocyte sedimentation rate. Slight allergic reactions were observed in 5 patients in the form of a rather widespread pruritus and small urticarial weals which subsided without treatment 30 minutes after the cessation of the transfusion. *A. Swan*

1285. **The Clinical Use of Dextran as a Plasma Substitute**
P. S. HETZEL. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 657–663, May 17, 1952. 3 figs., 12 refs.

Dextran is a plasma substitute, the crude form of which is a bacterial polysaccharide prepared from cultures of *Leuconostoc mesenteroides*. As isolated from these cultures it has a molecular weight of 4,000,000, and particles of this size when given intravenously cause glomerular and capillary damage. For infusion purposes, therefore, crude dextran is degraded by acid hydrolysis to produce particles of a molecular weight of 70,000 to 100,000, thus approximating the molecular weight of serum albumin (68,000). The present author reports 15 cases in which dextran was given for shock due to burns, dehydration, or operation and records its effects on the blood and on renal and hepatic function. In all cases shock was adequately combated, and no evidence of toxicity, no febrile reactions, and no sensitization phenomena were observed.

It has been shown by Bull *et al.* (*Lancet*, 1949, **1**, 134) that infusion of dextran causes a reduction in the plasma protein content, and in the present series estimations of the serum albumin : globulin ratio suggested that the serum globulin is the fraction affected. This specific withdrawal of globulin, the osmotic activity of which is much less than that of albumin, upsets the osmotic balance to a much smaller extent than a general loss of protein, and no permanent damage results. As soon as the dextran disappears from the circulation the globulin returns. This mechanism does not appear to be a specific effect of dextran, and is probably only a factor in preventing a gross overloading of the plasma.

Renal function was not as a rule impaired, but 2 patients developed lower nephron nephrosis from which they died, and which might have been due to the hypertonicity of the dextran solution. No specific change in liver function was detected. Five cases are described, including the 2 fatal cases. *S. M. Vassallo*

1286. **Resuscitation by Means of Endocarotid Transfusion Directed Cranially.** (La rianimazione con trasfusione endocarotidea in senso craniale)
A. M. DOGLIOTTI, A. CONSTANTINI, G. DEI POLI, and L. CALDAROLA. *Minerva Medica* [*Minerva med., Torino*] **43**, 893–896, April 30, 1952. 19 figs.

The authors demonstrated in experiments on dogs that transfusion of blood into the carotid artery, directed cranially, was followed by flooding of the cerebral vessels by the transfusion fluid and achieved a return of cardiac contraction in animals in a state of collapse with failure of the heart action. A similar transfusion of 120 to 150 ml. of blood had a similar effect on 3 human patients suffering from a severe degree of shock. *Ian Aird*

BONE AND JOINT SURGERY

1287. **Regeneration of the Menisci of the Knee after Meniscectomy.** (La régénération des ménisques du genou après méniscectomie)
J. MOREL, P. BASTIEN, and F. VANVELCENAHER. *Revue de Chirurgie Orthopédique et Réparatrice de l'Appareil Moteur* [*Rev. Chir. orthop.*] **38**, 137–153, April–June, 1952. 6 figs., bibliography.

The regeneration of the meniscus in the dog was first reported by Lenail in 1898, and in man in 1929 by Mandl. Regeneration may be complete or partial according to whether a total or partial meniscectomy has been performed, and the regenerated meniscus may suffer longitudinal or transverse tears.

Regeneration in animals has been studied in the guinea-pig, the dog, and the rabbit; the experiments reported here were on rabbits. After meniscectomy the animals were killed, and the results studied, at intervals varying from 1 to 13 months. From the first month there is regeneration in the form of a granulation-tissue pad, which during the second and third months assumes a trapezoidal shape with a narrow inner margin. In the fourth month the normal form of the meniscus is redeveloped and little subsequent change occurs. The new meniscus is paler, the surface less polished, and the consistence less firm than the normal meniscus. Histologically, during the first month there is a vascular granulation tissue with irregular disposition of cells; in the second to third months the peripheral zone appears much the same, but the inner zone shows a concentric orientation of fibres to the free border; in the fourth month there is a reduction in the cellular elements and cessation of peripheral activity, the blood vessels slowly become reduced in number, and the peripheral zone assumes the character of organized fibrous tissue.

The stimulating factors responsible for regeneration are uncertain, but regeneration appears to be due to a physiological need to cushion the articular margins of the joint; it is, however, inconstant in both man and animals. The new meniscus is composed of fibro-

cartilaginous tissue in the guinea-pig, of fibrous and sometimes fibro-cartilaginous tissue in the dog, and of tendinous tissue in the rabbit. In man the tissue is fibrous or sometimes fibro-cartilaginous, but the latter tissue requires considerable time to develop and is therefore related in its time of appearance to the age of the regenerated meniscus. Failure of regeneration in man may occur in about 6% of cases. The frequency of injury to the redeveloped meniscus is low owing to its reduced size and its broader attachment to the capsule. Probably sufficient displacement to injure the cartilage can occur only in unstable knees.

[In man, although the redevelopment of the meniscus is generally considered to occur relatively infrequently, it is nevertheless important, as total meniscectomy undoubtedly increases the frequency of marginal arthritic change. It would be valuable to know whether this change is in any way influenced by the redevelopment of the meniscus. If the regenerated meniscus exerted a favourable influence then some additional weight would be lent to the argument favouring total meniscectomy in almost all cases of cartilage injury. It is probable that redevelopment takes place only after total meniscectomy in man.] *J. G. Bonnin*

1288. **Jaw Tumours. III. Adamantinoma**
W. GIRDWOOD. *South African Medical Journal* [*S. Afr. med. J.*] **26**, 340–346, April 19, 1952. 23 figs., 26 refs.

Adamantinoma is the commonest lower-jaw tumour, especially in the Bantu, in whom the growth often reaches a large size before advice is taken. Most of the tumours are cystic, but solid and all intermediate forms occur, the histological patterns being very variable. The author describes six groups: (1) peripheral alveolar type; (2) central adamantinoma of the horizontal ramus, with thinning of the mandible to a thin rim; (3) symphysial adamantinoma; (4) adamantinoma of the ascending ramus; (5) massive adamantinoma; (6) adamantinoma of the upper jaw.

Tumours of Group 1 may be removed by local excision, with chemical cauterization of the cavity. But in Groups 2, 3, 4, and 5 more extensive excision is required, a varying amount of the mandible being removed; a prosthesis and bone graft are frequently necessary afterwards. The tumours of Group 6 are usually solid, and behave in a manner indistinguishable from carcinoma of the antrum; in this group only palliative treatment is possible. *A. G. Beckett*

1289. **Stenosing Tenovaginitis at the Wrist and Fingers. Report of 423 Cases in 369 Patients with 354 Operations**
P. W. LAPIDUS and R. FENTON. *Archives of Surgery* [*Arch. Surg., Chicago*] **64**, 475–487, April, 1952. 2 figs., 4 refs.

Attention is called to frequently occurring stenosing tenovaginitis at the radial styloid and at the flexor sheath of the fingers, which are often misdiagnosed. A series of 369 patients with 423 sheaths involved and 354 operations performed, is analysed. In a great majority the condition is an occupational one and, therefore, compensable in the industrial workers.

Although spontaneous recovery may occur, operative release is preferable, particularly when symptoms are present more than one month. Operative technique is described; the importance of skin incisions along the skin creases (transverse at the radial styloid), suturing of the skin only, and immediate postoperative mobilization, is emphasized.—[Authors' summary.]

1290. **Hallux Valgus: Predisposing Anatomical Causes**
R. H. HARDY and J. C. R. CLAPHAM. *Lancet* [*Lancet*] **1**, 1180–1183, June 14, 1952. 3 figs., 6 refs.

Radiographs of the feet of nearly 2,000 school-children were examined to elucidate the aetiology of hallux valgus. It was found that hallux valgus preceded widening of the angle between the first and second metatarsals, and it is concluded that congenital widening of the intermetatarsal angle cannot be the cause of hallux valgus.
George Perkins

PHYSIOTHERAPY

1291. **Advantages and Limitations of Ultrasonics in Medicine**
H. P. SCHWAN and E. L. CARSTENSEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **149**, 121–125, May 10, 1952. 5 figs., 13 refs.

The authors explain briefly the physics and some of the biophysical problems involved in the production of heat by ultrasonics in tissues and other media. As a sound wave travels through a medium a definite fraction of the energy is absorbed in the form of heat. For example, the absorption in muscle is about twice that in fat; this is a definite advantage of ultrasonic heating over electromagnetic diathermy in which the maximum heat production is in the fatty tissue.

Since ultrasound is simply a mechanical vibration its effects on biological material are necessarily of a physical nature. The effects are either thermal or non-thermal, and both may play a significant role in treatment. The non-thermal effects can produce increased permeability of membranes. This is explained by the "stirring" action of sound on the solution on both sides of the membrane, and the consequent increase in the gradient of the ion concentration near the membrane. Another non-thermal effect is the resonant oscillation of gas bubbles in liquid, which can be responsible for the destruction of cells in the tissues. High intensities of sound may produce changes of state in the medium by the formation of gaseous cavitation and the breaking up of long-chain molecules.

After comparing the characteristics and advantages of ultrasound and microwave diathermy the authors decide in favour of ultrasound on the following grounds: ultrasound therapy has good beaming properties, efficiently transfers energy from the source to the tissue, and has good depth of penetration and selective heating effect at the interspaces. It is emphasized, however, that care must be exercised in its use as the therapeutic indications are not yet well established.
M. H. L. Desmarais

Neurology and Neurosurgery

1292. **Thymectomy in the Treatment of Myasthenia Gravis**
R. T. Ross. *Lancet* [*Lancet*] **1**, 785–787, April 19, 1952. 9 refs.

The effect of thymectomy on 100 patients with simple hyperplasia of the thymus (73 females, 27 males) is reported. The age of the patient at onset of the disease had no effect on the result of the operation, but the interval which elapsed between the onset of the disease and operation was important, the shorter the interval the better being the result. After an average period of 4½ years, improvement (varying from complete relief of symptoms to a reduction in the daily requirement of neostigmine) was noted in 87 patients. It is claimed that these results are better than those obtained with medical treatment alone. *Lambert Rogers*

1293. **Head-dropping Test**
R. Wartenberg. *British Medical Journal* [*Brit. med. J.*] **1**, 687–689, March 29, 1952. 1 fig., 10 refs.

The author, after a lengthy review of the well-known features of Parkinsonism, sets forth at almost equal length the technique and merits of his so-called "head-dropping test". This is carried out with the patient lying on his back, his head resting in the palm of the examiner's hand. When relaxation has been achieved the head is sharply lifted and allowed to fall back on to the hand. "A slow hesitant movement or a soft fall, a gentle hitting of the surface, is indicative of a lesion of the extrapyramidal system." [The particular merits of this test remain obscure.] *J. St. C. Elkington*

CEREBRAL VASCULAR SYSTEM

1294. **Cerebral Apoplexy due to Spontaneous Intracranial Hemorrhage. Report of Twenty-three Cases**
M. Scott. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **149**, 129–136, May 10, 1952. 6 figs., 22 refs.

The author reports on 23 cases operated on by him for spontaneous, non-traumatic, intracranial haemorrhage. The ages of the patients ranged from 25 to 70; 12 of them (52%) had systemic hypertension. The haemorrhage had occurred into the internal capsule in 9 cases, into the frontal lobe in 4, and into the temporal lobe in 7; 3 cases had a subdural haematoma. Biopsy of the haematoma wall was performed in 22 cases. In 17 there was no obvious cause for the haemorrhage; rupture of an artery, without visible aneurysm, was seen in 3; in one an aneurysm of the middle cerebral artery had ruptured; and in 2 cases haemorrhage had occurred into metastatic tumours.

The symptomatology and the differential diagnosis between haemorrhage and thrombosis are briefly discussed: 9 patients were in stupor or coma on admission to the hospital, and 4 of the 8 deaths occurred in this group. The pressure of the cerebrospinal fluid was raised in 18 (90%) of 20 cases examined, though the average intracranial pressure was only 238 mm. of water; the spinal fluid was bloodstained in 14 out of 19 cases (73%). Exploratory craniotomy was performed in 14 cases, but in the remaining 9 cases enlarged trephine holes were adequate. The mortality (8 cases) was 35% for the whole group, and 28% if the 2 cases with metastatic tumours are excluded. Of the 15 survivors, 5 have resumed work, 2 can do only light housework, 5 have remained hemiplegic, one could not be traced, and 2 died within 2½ years.

The indications for surgical intervention are reviewed. The most important of these are: (1) progressive deepening of stupor; (2) progressive slowing of the pulse; (3) signs of raised intracranial pressure; (4) displacement of the calcified pineal gland, seen radiologically; (5) displacement of cerebral vessels on angiography, in the presence of localizing cerebral signs of sudden onset. [The importance of angiography is perhaps not sufficiently stressed.] *J. Foley*

1295. **Cerebral Vascular Complications of Metastatic Carcinoma**
L. Madow and B. J. Alpers. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **11**, 137–148, April, 1952. 5 figs., 17 refs.

The authors report, from Jefferson Medical College, Philadelphia, 2 cases of metastatic carcinoma showing unusual effects of intracranial metastasis. The first was in a man of 49 years who became ill after the extraction of several infected teeth and was thought to have multiple abscesses in the right cerebral hemisphere. His illness followed a relapsing course, and he died before ventriculography could be carried out. Post mortem he was found to have a primary squamous-cell carcinoma of the lung with metastases to the liver, kidneys, adrenal glands, heart, entire small bowel mucosa, vertebrae, and the mediastinal, mesenteric, and omental lymph nodes. There were no nodules in the brain, but several regions were pale, and though some of the cerebral blood vessels were engorged and dilated, no areas of softening were palpated. A number of sections were made of the brain, and when zones of softening were found these were sectioned serially. The meninges were normal, but in the cortical blood vessels many plugs of carcinomatous tissue were seen, some of which were surrounded by fibrinous clot which fixed them within the vessels, but many were lying quite free in the lumen. There was complete destruction of the cortical architecture in three areas of the right side, involving the gyrus rectus, the pre-motor cortex, and the parietal lobe. The cerebral cortex in general showed enlargement of the peri-

vascular spaces. No lesions were found in other parts of the brain.

The second case was that of a woman of 50 who developed a lump in the left tibia which proved to be a metastasis from a hypernephroma of the right kidney. Both lesions were removed successfully, but 17 months later she suddenly became comatose and died. Necropsy showed some blood clot at the base of the brain, but principally a large intraventricular haemorrhage involving the left lateral and third and fourth ventricles. There was a single tumour nodule in the choroid plexus of the left lateral ventricle invading the surrounding white matter, and some softening of the centrum ovale. Histological section of the tumour nodule showed cells with a small round nucleus usually containing one or two chromatin dots and a stout nuclear membrane; the cytoplasm had a distinct cellular membrane and was cuboidal in shape. No other metastases were found at necropsy. *Donald McDonald*

1296. **Preliminary Trials of Certain Ganglionic Blocking Agents in the Treatment of Acute Cerebral Vascular Accidents.** (Premiers essais d'application de certains ganglioplégiques aux accidents vasculaires aigus du cerveau)

D. Petit-Dutaillis, G. Guiot, and B. Damoiseau. *Presse Médicale* [*Pr. méd.*] **60**, 657–659, May 7, 1952. 2 refs.

The authors, having noted the success with which the various ganglion-blocking agents, such as hexamethonium, have been used in neurosurgery to reduce haemorrhage and cerebral oedema, have tried the effect of these drugs in a case of cerebral haemorrhage and 2 cases of cerebral thrombosis; the preparation used was " pendiomide ". One case of eclampsia was also treated with hexamethonium. The results were favourable, but more trials are needed before the true value of these drugs in cerebro-vascular disease accompanied by hypertension can be determined. To be effective, treatment must be started early, as soon after the accident as possible, and after not more than 24 hours.

G. S. Crockett

CEREBRAL TUMOURS

1297. **Hemangiomas of the Fourth Ventricle**

A. E. Walker, H. C. Johnson, and K. M. Browne. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **11**, 103–115, April, 1952. 8 figs., 11 refs.

From Johns Hopkins Hospital, Baltimore, 5 new cases of tumours of blood vessels extending into the fourth ventricle are reported. The first was in a man aged 45 who complained of headache and staggering gait. He had a raised intracranial pressure, and ventriculography showed symmetrical dilatation with a filling defect in the caudal part of the fourth ventricle. The tumour was removed surgically, but the patient died on the 10th post-operative day. The tumour was heterogeneous in character, some areas being filled with cells looking like regularly arranged astrocytes. Nearer the periphery the tumour was very vascular and contained blood vessels of all types ranging in size from thin-walled capillaries up to irregular racemose and cavernous spaces 50 to 150 μ in diameter. Around the tumour most of the vessels were thick-walled and 10 to 20 μ in diameter.

The second patient was a child of 22 months who had symptoms suggestive of an inoperable brain-stem tumour. This case was first treated with deep *x*-ray therapy, but subsequently developed raised intracranial pressure; when the posterior fossa was explored a vascular tumour was seen on the floor of the fourth ventricle. Examination of a biopsy specimen suggested a haemangioma, but it might have been from a very vascular area of a glioma. The remaining cases had been operated on by another surgeon in 1925, 1935, and 1933 respectively. One of these was in a boy aged 16; here the tumour invaded the pons, and consisted of a mass of large, thin-walled, sinusoidal channels. The 4th patient died 11 years after operation, and was found to have a haemangioma extending from the dorsal portion of the pons throughout the fourth ventricle and compressing the cerebellum; a diversity of cells similar to that of the first case was seen. The fifth patient had a tumour in the posterior half of the fourth ventricle; the tumour was totally removed, but the patient died one hour later. Histologically, it was found to be a haemangioblastoma.

The authors emphasize the difficulty of diagnosing the precise type of tumour from its macroscopic appearance. They also lay stress on the extensive changes in the intervascular tissue. These changes, such as glial proliferation and necrosis, are considered to result from the normal and abnormal development of immature neural tissue included with the vascular anomaly in early foetal life. *Donald McDonald*

EPILEPSY

1298. **Forced Thinking as Part of the Epileptic Attack**

I. M. Allen. *New Zealand Medical Journal* [*N.Z. med. J.*] **51**, 86–95, April, 1952. 6 refs.

In 10 out of a series of 500 cases of epilepsy, the records of which were analysed by the author, forced thinking was a prominent feature, appearing as an early, but not always the initial, symptom in slowly developing attacks, though not being apparent in those starting rapidly with sudden unconsciousness. The occurrence of forced thinking was recalled after the attack in all cases, but the thought content was remembered by only 2 patients, one of whom could recall only one thought which recurred more often than any other, while the other invariably had the same thought, which was associated with compulsive movement of the eyes to look at a number of objects in turn. In another case the patient knew that he argued with himself, but could not remember the subject of the argument, while in others the general nature of the thought, such as " something past " or " something weird and strange " could be described. In one case the thought " came as if a voice was speaking ". The forced thinking was preceded by an epigastric sensation in 2 cases, and was accompanied in others by a feeling

of pleasure or interest. It was followed by a simple adversive seizure in 2 cases, by spontaneous sensation in the limbs and trunk on one side in 2 others, and by loss of muscle tone in another. It was followed immediately by unconsciousness in some attacks in 5 cases, with loss of muscle tone and falling, and then stiffness and occasionally clonic movements.

The symptoms occurring before, with, or after forced thinking thus gave only a very general indication of the site of the initial discharge. More significant were the symptoms which did not appear—there were none pointing to the neighbourhood of the visuosensory cortex, the temporal lobe, or the parietal lobe, no vertiginous symptoms suggesting an initial discharge in the parietal lobe close to the midline or in recognized motor areas on the convexity of the cerebral hemisphere, in the supplementary motor area on the inner aspect of the primary motor area for the foot, or in the frontal lobe in front of the lower part of the precentral gyrus. It is held that when forced thinking is an early symptom of an epileptic attack the site of the initial discharge must be in a part of the frontal lobe near the midline, in front of the precentral gyrus and appreciably behind the frontal pole, and must be unilateral. As it has not been shown that a discharge within neuronal circuits can produce thought processes, the similarity between forced thinking and automatic coordinated movements, and the fact that the two symptoms sometimes appear in sequence, make it seem probable that the former arises as an indirect effect due to release from higher control of lower, but complex, levels of integration of which the thought content and its emotional accompaniment are part.

Myra Mackenzie

SPINAL CORD

1299. **Low Back Pain due to Anomalies of the Epidural Vessels. Pathology of the Intraspinal Venous Plexus.** (Lombosciatiques par anomalies vasculaires épidurales. Contribution à l'étude de la pathologie du plexus veineux intrarachidien)
P. Gloor, E. Woringer, J. Schneider, and G. Brogly. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **82**, 537–542, May 17, 1952. Bibliography.

In this paper, from the Pasteur Hospital, Colmar, the authors review 181 cases of low back pain in which they have operated since 1948. They found that in 136 cases (75%) the cause was herniation of a vertebral disk; the remaining 45 cases were due to a variety of causes, the most frequently occurring being varicosities of the epidural vessels, which occurred in 12 (6·2%) of their cases. The clinical picture and myelographic appearance in these cases closely resembled those in the cases due to herniated disk, for in both lesions the radicular pain is of mechanical origin, the abnormally dilated epidural vessels acting like an extruded disk to cause pressure on the spinal roots. That this occurs most frequently at the level of L5–S1 may be explained by the anatomical fact that the spinal roots are in the closest contact with the anterior surface of the spinal canal at this level, and are thus more exposed to pressure than at other levels. Discussing the causation of the varicosity, the authors suggest that all conditions which raise the intra-abdominal or intrathoracic pressure, either acutely and repeatedly or continuously, can lead to the formation of epidural venous dilatations.

In the authors' opinion the differential diagnosis of epidural varicosity from herniated disk cannot be made before operation. In both cases the clinical picture is very similar, and the radiographs show the same notch at the point of pressure. They add the warning that a herniated disk and epidural varicosity may both be present in the same patient, as they found in a number of their cases. In a note on contrast media the authors deprecate the use of iodized oil for myelography in cases of sciatica because of the pain it may cause. It may advantageously be replaced by sodium mono-iodomethane sulphonate, as has been pointed out by Woringer and others; this substance produces no undesirable effect and gives good radiographic definition. *E. Forrai*

1300. **Radiculitis of the Cervical Spine. Simulation of Coronary Conditions and Physical Treatment**
H. I. Weiser. *British Journal of Physical Medicine* [*Brit. J. phys. Med.*] **15**, 105–107, May, 1952. 9 refs.

1301. **Trypan Blue and Trypan Red in the Treatment of Amyotrophic Lateral Sclerosis. Their Application to the Treatment of Disseminated Sclerosis.** (Le bleu et le rouge trypan dans le traitement de la sclérose latérale amyotrophique. Application au traitement de la sclérose en plaques)
R. A. Schwob and M. Bonduelle. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **28**, 1637–1642, May 26, 1952.

An account is given of the treatment of 11 cases of amyotrophic lateral sclerosis and 12 cases of disseminated sclerosis by the intravenous injection of solutions of trypan red or trypan blue. The treatment is based on the hypothesis that amyotrophic lateral sclerosis may be due to a blood-borne toxin which reaches the nervous system through the blood–brain barrier, and on the work of Aird (*Arch. Neurol. Psychiat., Chicago*, 1948, **59**, 779), who showed that trypan red given intravenously diminishes the permeability of the blood–brain barrier.

The dyes were given in doses of 5 to 10 ml. of a 1% solution in water, an initial series being given at 2-day intervals to produce a perceptible coloration of the skin and mucosae, and subsequent doses frequently enough to maintain the coloration. The injections were repeated over long periods, in one case up to 2 years. The authors claim that the progress of the disease was arrested in 3 of the 11 cases of amyotrophic lateral sclerosis and slowed down in 2. The treatment failed in the remaining 6 cases. The treatment of the 12 cases of disseminated sclerosis was continued for one year, during which time the impression gained was that rapidly successive relapses were arrested in 3 cases.

[This is not a convincing paper, as the authors appear to be aware. The unpredictable course of the disease in

amyotrophic lateral sclerosis, and even more so in disseminated sclerosis, makes it impossible to assess the value of any treatment, whatever its basis, on the findings in a small number of cases observed over a short period.]

J. MacD. Holmes

DISSEMINATED SCLEROSIS

1302. Multiple Sclerosis in Rural Norway

R. L. SWANK, O. LERSTAD, A. STROM, and J. BACKER. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 721–728, May 8, 1952. 1 fig., 20 refs.

One of the authors has previously suggested (Swank, *Amer, J. med. Sci.*, 1950, **220**, 421) that the amount, and possibly the nature, of fat consumption may be related to the varying incidence of disseminated sclerosis. A survey was carried out in Norway of patients in whom a diagnosis of disseminated sclerosis was made between 1935 and 1948. The nutritional status of inhabitants of 7 rural districts was studied. The impression gained was that there was a high incidence of disseminated sclerosis in Norway among farm and dairy workers, though it was admitted that from a statistical point of view the material was small and possibly not completely representative. The investigation also indicated that in those areas where the incidence of disseminated sclerosis was high, not only was the fat intake high, but so also was the intake of milk and of animal fat. The authors suggest that the ingestion of fat may be among the factors that precipitate disseminated sclerosis in susceptible persons.

Hugh Garland

1303. The Ocular Manifestations of Disseminated Sclerosis

K. C. WYBAR. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **45**, 315–320, May, 1952. 1 fig., 9 refs.

The author discusses the signs and symptoms occurring in the eyes of 91 consecutive patients with disseminated sclerosis seen at the Western Infirmary, Glasgow, and describes a modification of Stern's method of detecting subclinical changes in pupillary function. The ocular findings were as follows: retrobulbar neuritis had occurred in 25 cases, being the earliest manifestation in 19. Diplopia had been the presenting symptom in 14 of 28 cases; only 2 patients had both diplopia and retrobulbar neuritis. Ptosis was present in 2, nystagmus in 57, and involvement of ocular movement in 9 of the cases. Pallor of the optic disks was seen in 23 cases. The average size of the pupil was not found to diverge from the normal to a significant degree. Spontaneous hippus was observed in 33 cases. Gross changes in the light reflex were found in 4 cases, and impairment of accommodation in 2. In 19 cases there was a possible abnormality of the light reflex.

Stern's method (*Brit. J. Ophthal.*, 1944, **28**, 275) of testing pupillary reactions was carried out with slight modification in 90 cases of the series. In this method oscillations of the pupil are induced, in a darkened room, by shining a pin-point beam of light (the author used a vertical focused beam) just within the margin of the pupil. The latter contracts and after a short latent period dilates again; repetition of this process gives rise to the oscillations. A chin rest is used and the patient is asked to fix his eyes on a weak source of light behind the examiner's head. With the corneal microscope observations were made of the rate, rhythm, and amplitude of the oscillations. During an acute attack of retrobulbar neuritis 2 eyes showed worm-like contractions of the pupillary margin. No oscillations occurred in one case of internal ophthalmoplegia. Deviations from normal values, notably a reduction in amplitude and number of oscillations, were observed in 70 of the remaining 177 eyes; among these were 31 in which the pupil had reacted sluggishly to light. A brief summary of the physiology of pupillary control is given; the lesion was located in the afferent pathway in 17 of the pupils examined.

R. Emery

1304. Chronic Neurological Disease as a Possible Form of Lead Poisoning

E. J. BUTLER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **15**, 119–128, May, 1952. 34 refs.

The author briefly reviews the evidence which has been brought forward from time to time in support of the hypothesis that lead may be an aetiological factor of significance in disseminated sclerosis. It is pointed out that in large measure this evidence is circumstantial, and that even where increased skeletal deposits of lead occur in association with disseminated sclerosis they do not necessarily indicate intoxication. On the other hand, no reliable analytical investigation has hitherto been undertaken to prove or disprove the hypothesis, and the present author therefore made a most careful analysis of the lead content of the tissues and body fluids in 31 cases of disseminated sclerosis. For comparison, similar estimations were made in 56 cases of other chronic neurological diseases, on 7 patients without specific symptoms but with a history of exposure to lead, and in 4 cases of industrial lead poisoning.

The urinary excretion of lead of all the patients with neurological disease was within normal limits. It was also noted that the high urinary copper excretion of Wilson's disease was not accompanied by abnormal lead excretion. Administration of BAL to patients with neurological disease produced an increase in lead excretion, but this had no apparent relation to any particular disease, nor did it indicate the presence of abnormal amounts of lead in the circulation or soft tissues. In the cases of lead poisoning a great increase in coproporphyrin excretion was found: this did not occur in patients with disseminated sclerosis or other neurological disease. The lead content of the cerebrospinal fluid was not increased in the neurological cases—nor in patients with lead colic. Comparison of the lead content of skeletal tissue, liver, cerebral white matter, and spinal cord showed no abnormal concentration in the nervous tissues and no abnormality in the distribution of lead as between skeletal and soft tissues in disseminated sclerosis.

J. C. Brocklehurst

Psychiatry

PSYCHOSOMATIC MEDICINE

1305. **Psychiatric Findings in Crohn's Disease**
R. W. CROCKET. *Lancet* [*Lancet*] **1**, 946–949, May 10, 1952. 20 refs.

In a previous study of patients with Crohn's disease the prominence of neurotic traits had been noted. In continuation of this investigation at Leeds General Infirmary, 16 patients with regional ileitis were given a psychiatric examination. In 2 patients anxiety had been associated with diarrhoea on some occasions at least; in another diarrhoea was a regular concomitant of stress; 9 patients showed anxiety traits in adult life, and 8 gave a history of anxiety in childhood. These findings did not differ greatly from the incidence of chronic anxiety in comparable groups of hospital patients with other disorders. Only 5 of the 16 patients recognized subjectively a relationship between emotional stress and the symptoms of regional ileitis, and 2 of these did so only after operation. Neither immaturity nor dependency appeared unduly prominent in these patients. Obsessional traits were obvious in 6 patients, but only in 3 did they cause distress.

[The psychiatric examination was limited to one interview. No projection tests were applied, the patient's relatives were not interviewed, and the patient was not kept under observation for a reasonable period to allow of an assessment of his reactions to life situations and the relationship of symptoms to stress. The negative finding that immaturity and dependency were not prominent is thus of little value. Quite commonly patients with stress disorders do not know, at the first interview, what brings their symptoms on; this does not show that stress is not important, but merely that they have, at that time, no insight.] *Desmond O'Neill*

1306. **Uterine Bleeding in Tension States**
D. O'NEILL. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **59**, 234–239, April, 1952. 6 refs.

The cases of 12 women complaining of excessive uterine bleeding due to a tension state are reported, and an attempt is made to formulate the pathogenetic pattern of this condition. The type of disturbance of the menses varied, some patients complaining of flooding, some of prolongation of the periods, and some of excessive frequency or intermenstrual bleeding. The patients, 6 of whom were parous, were all between 22 and 35 years old except for one woman of 49. In only one case was a physical abnormality (fibroids) present that could have caused the condition, but in this case the menorrhagia was clearly related to emotional tension and ceased with restoration of tranquillity. In all cases there was a clear correlation between onset of bleeding and emotional tension, and in 5 cases discrete attacks repeatedly followed individual experiences of stress. Sex difficulties were directly responsible in 4 cases; jealousy, resentment, grief, and guilt preceded the condition in 5; and in 2 it was related to a heavy burden of responsibility at work. Relief of the emotional tension or change of environment resulted in a return of normal menstrual function in most cases. Other symptoms associated with the bleeding were depression, anxiety, fatigue, headache, insomnia, and lassitude, the first two being the predominant emotional states.

The author emphasizes that uterine bleeding of emotional origin occurs as part of the " Atalanta syndrome ", which also includes frigidity, dyspareunia, other disorders of menstruation, and disorders of parity, and which is found in at least some women with a masculine identification. Such unconscious repudiation of femininity was three times more common among the parous women in this series than would normally be expected.
E. H. Johnson

PSYCHONEUROSIS

1307. **" Hysteria " in Men. A Study of 38 Patients so Diagnosed and 194 Control Subjects**
E. ROBINS, J. J. PURTELL, and M. E. COHEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **246**, 677–685, May 1, 1952. Bibliography.

A study was made at the Massachusetts General Hospital and other hospitals of 38 men who had been diagnosed by others than the authors as having hysteria, " conversion reaction ", or " neurosis "; the patients had no other diagnosis, and showed at least one of the following signs or symptoms: amnesia, fits, unexplained pain, vomiting, urinary retention, blindness, paralysis, trances, impotence, or aphonia. Control groups consisted of 39 healthy men, 31 men with chronic medical illnesses, 99 men with anxiety neurosis, and 25 women with hysteria.

The authors define " hysteria " in men as differing from hysteria in women in that it is of later onset, the possibility of material gain is present, the symptoms are fewer, the men are less dramatic and less vague in describing their symptoms, have less frequent hospitalization, and indulge in no excessive surgery. The commonest symptoms in men were musculo-skeletal pains, abdominal pain, nausea, vomiting, nervousness, headache, " being easily upset ", giddy spells, dyspnoea, and palpitation, and in addition at least one of the following: amnesia, blindness, fits, trances, various localized pains, paralysis, impotence, or aphonia. In the authors' view the diagnosis of hysteria in men when no possibility of material gain exists is probably inaccurate. A number of cases of organic disease were referred to the authors

for " hysteria "; these included cerebral embolus with aphasia, tetanus, epilepsy, catatonic schizophrenia, gastric carcinoma, torticollis, multiple sclerosis, poliomyelitis, and retrobulbar neuritis.

The mean age of onset in the men (all ex-servicemen) was 25·7 years and in the women 16·9 years; the mean number of symptoms in men was 11, in women 20; of the men, 26% had been thought to be malingering, whereas only 9% of the women had been so suspected; 68% of the men thought they had been helped by treatment, but only 18% of the women did so. It was noted that 29% of the women, but none of the men, took opiates or barbiturates. The authors compare the patients with hysteria with their control groups of healthy men, men with chronic medical illnesses, and men with anxiety neurosis, and point out the significant differences.

[All the men with hysteria were ex-servicemen. The outlook of pensioners, especially when they are in-patients as were these, is very different from that of non-pensioners. This difference may account for some or all of the symptoms of this " hysteria ".]

G. de M. Rudolf

1308. **Evaluation of Carbon Dioxide Therapy of Neuroses** A. J. JACKMAN and C. A. SCHORR. *Journal of Clinical and Experimental Psychopathology* [*J. clin. exp. Psychopath.*] **13**, 17–30, Jan.–March, 1952. 12 refs.

With the object of making a critical evaluation of carbon dioxide inhalation in the treatment of neuroses the authors carried out clinical psychiatric examinations and tests on three groups of patients: (1) 10 patients examined before, and again 10 days after, a full course of treatment with 30% carbon dioxide in oxygen; (2) 10 patients examined before, and again 2 to 29 months after, a similar course; and (3) 5 patients examined before, and again 10 days after, a course of inhalations of air with non-therapeutic concentrations of carbon dioxide, the patients being led to believe that they were receiving the same treatment as those in the other groups. This last group consisted of men only, the others each including 3 women. The patients' ages ranged from 21 to 42 years and (apart from one patient who received 300) the number of treatments given ranged from 7 to 79, the most common number being 30. The method of treatment consisted in giving the gas mixture through a face mask at a pressure of 2 lb. per sq. in. (140 g. per sq. cm.) until unconsciousness occurred (or for 30 inhalations in the control group). Treatment, which was given on alternate days, took about 2 minutes, and recovery about 5 to 10 minutes. The patients returned to work immediately.

A numerical assessment of symptoms present before and after treatment in each case showed that in 19 of the 20 patients in Groups 1 and 2 the symptoms decreased, whereas of the 5 control subjects only 2 showed a decrease. The authors therefore regard this form of treatment as " extremely effective ", as well as safe: during the administration of over 4,000 treatments in 100 cases the only complications encountered by the senior author were enuresis occurring at the beginning of treatment in 6 cases, mild convulsions in 4, and slight lacerations of the lips or buccal mucous membrane in 6. The hypothesis is advanced that this form of therapy operates in much the same manner as frontal lobotomy, the authors being of the opinion that it causes organic changes in the brain.

[The figures show that the period of treatment in Groups 1 and 2 ranged from 4 weeks to nearly 2 years, in the majority of cases being about 10 weeks. The percentage of symptoms remaining after treatment ranged from 4 to 100 (the latter being in one patient only). Five patients retained over one-fourth of their symptoms, and a further 5 over one-half.] *G. de M. Rudolf*

DRUG ADDICTION AND ALCOHOLISM

1309. **Treatment of Drug Addiction. Preliminary Report** E. Y. WILLIAMS. *Psychiatric Quarterly* [*Psychiat. Quart.*] **25**, 604–612, 1951. 18 refs.

At Freedmen's Hospital, Washington, D.C., 16 cases of drug addiction were treated with calcium gluconate, given alone (8 cases), in combination with barbiturates (7 cases), or (in one case) in combination with nicotinic acid. The method was as follows: morphine and its derivatives were abruptly withdrawn, and for the first 2 days the patients received 10 ml. of a 10 to 20% solution of calcium gluconate (to which 2 gr. (0·13 g.) of barbiturate was added in 7 cases) intravenously every 4 hours; the frequency was then reduced to 4 doses per day for the next 3 days, and to 3 doses per day for the following 3 or 4 days.

Immediate relief followed administration of calcium gluconate, but was of short duration and it was necessary to repeat the dose. Anxiety symptoms which appear after the cessation of withdrawal symptoms are said to be equally relieved by the preparation. In addition, dehydration was corrected and ascorbic acid and aneurin also given. The length of treatment, determined by the patient's degree of inanition or other physical disorders, usually did not exceed 4 weeks. Psychotherapy was also employed. *Catherine Schöpflin*

1310. **Purposeful Inhalation of Gasoline Vapors** O. W. CLINGER and N. A. JOHNSON. *Psychiatric Quarterly* [*Psychiat. Quart.*] **25**, 557–567, 1951. 3 refs.

The authors report the cases of 2 adolescent boys who engaged in inhalation of petrol vapour. One, a 16-year-old negro boy, exhibited definite schizophrenic symptoms and the other, a 13-year-old white boy, had a schizoid personality. Both boys used this habit as a means of escape from reality and both experienced pleasurable hallucinations (associated with sexual fantasies in the first case certainly and probably in the second also). In the negro boy the habit had developed into addiction 3 years before his admission to hospital. During his stay in hospital, where he was treated for schizophrenia, it was revealed that inhalation of petrol vapour was a common practice among the boys in his community. Addiction was proved only in this boy, in whom the sporadic practice was probably due at first to

maladjustment preceding the onset of schizophrenia, but grew into addiction with the manifestation of the schizophrenia.

The second boy, of an entirely different community, had engaged in inhalation of petrol vapour for about a year before he was examined; he showed rapid improvement in his symptoms of maladjustment and of withdrawal from reality when treated by psychotherapy. The authors emphasize that the occurrence of such a practice may be more common than is realized, but that persistence in the habit indicates that pre-existing defects in personality are present. *Catherine Schöpflin*

1311. **Evaluation of Antidotes for the Alcohol Reaction Syndrome in Patients Treated with Disulfiram (Tetraethylthiuram Disulfide)**
D. LESTER, E. J. CONWAY, and N. M. MANN. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **13**, 1–8, March, 1952. 2 figs., 6 refs.

At the Blue Hills Clinic of the Connecticut Commission on Alcoholism the authors investigated the effect of certain preparations on the reaction resulting from the absorption of alcohol in patients treated with tetraethylthiuram disulphide (" antabuse "). The preparations tested were: (1) saccharated iron oxide (1 patient); (2) a solution of ferrous chloride and ascorbic acid at *p*H 3 (2 patients); (3) a similar solution adjusted to *p*H 6·5 (6 patients); and (4) ascorbic acid alone (4 patients, 2 of whom had previously received Preparation 2). The dose of antabuse given daily was 20 mg. per kg. body weight orally for 4 days, and 10 mg. per kg. thereafter.

On the 5th, 12th, and in some instances the 19th days of treatment the patients were given a dose of alcohol which resulted in a maximum blood concentration of 20 to 25 mg. per 100 ml. Before or immediately after the ingestion of alcohol an intravenous infusion of 5% glucose in normal saline was started, and before and every 10 or 15 minutes after the administration of alcohol blood pressure, pulse and respiration rates, and presence or absence of flushing were recorded and capillary blood samples were taken for determination of alcohol and acetaldehyde content. The drug under test was given immediately before, and again 30 minutes after, the dose of alcohol given on the 12th day, the test on the 5th day providing control observations, and an additional therapeutic test being made in a few cases on the 19th day.

None of the preparations tested caused any reduction in the clinical features of the reaction or in the blood acetaldehyde levels, while the more acid preparation of iron and ascorbic acid appeared to aggravate the reaction, presumably owing to its acidity. It was noted in 2 cases that the vasomotor dysfunction which characterizes the reaction was most intense at a time when the blood acetaldehyde level was low, and it is pointed out that vasomotor collapse in such cases cannot be counteracted by measures designed to lower the acetaldehyde concentration of the blood, but that measures must be adopted which alleviate the symptoms and counteract shock. *Catherine Schöpflin*

1312. **Studies in Chronic Alcoholism: I. The Clinical Findings in 78 Cases of Chronic Alcoholism**
R. A. JOSKE and C. N. TURNER. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 729–734, May 31, 1952. 2 figs., 11 refs.

The authors review the clinical findings in 78 cases of chronic alcoholism (56 in males, 22 in females) treated at the Royal Melbourne Hospital during the 4-year period from 1947 to 1950. A detailed clinical examination of each patient was carried out, including inquiry into the clinical and dietetic history and radiological, biochemical, and pathological investigations when indicated, and all were followed up after discharge. The patients' ages ranged from 29 to 73, the main incidence being in the fifth decade in both sexes. Signs and symptoms were very varied, involving nearly the whole field of medicine, but malnutrition was the principal causative factor. Out of 54 reliable dietetic histories obtained, only 2 showed an adequate diet.

Only in 29 cases was the clinical history considered reliable. The most frequent presenting symptoms were abdominal pain, haematemesis, ataxia, jaundice, swelling of the abdomen, and psychotic episodes. Evidence of nutritional hepatitis was found in 51 cases, of peripheral neuritis in 33, and of central nervous lesions in 31, both central and peripheral lesions being present in 18 cases. Mental confusion occurred in 12 cases, delusions (including delirium tremens) in 10, and Korsakoff's psychosis in 4. Most of the patients were dirty and unkempt and vitamin-deficiency symptoms were common, including glossitis and angular stomatitis, one case of scurvy, one of pellagra, and 5 of wet beriberi with congestive cardiac failure. Other findings were gross oral sepsis (14), urinary infection (6), otitis media (1), acute arthritis (1), and extensive varicose ulceration (2). Lung affections (including bronchitis, hypostatic congestion, lobar pneumonia, bronchopneumonia, and asthma) occurred in 15 cases, but although radiographs were taken in all cases, tuberculosis was found in only one.

Myra Mackenzie

1313. **Studies in Chronic Alcoholism: II. A Social Study of Chronic Alcoholism**
E. G. SAINT and M. A. MACKAY. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 734–738, May 31, 1952. 2 refs.

A full social history was taken in 59 of the 78 cases of chronic alcoholism treated at the Royal Melbourne Hospital (see Abstract 1312), and a psychiatric assessment was subsequently made in 30 of these cases. Most of the patients came from the " hospital " classes, only 4 being of the professional class. Approximately one-half were unskilled or unemployed workers. Changes of occupation were frequent and, except in 2 cases, were in a socially downward direction. The 30 patients subjected to assessment of personality were classified as follows: (1) Normal, 12 cases; though excessive drinking is hardly normal behaviour, these persons were fairly well balanced, had moderate insight, and responded reasonably well to simple treatment. (2) " Subcultural " or mentally defective, 7 cases; these patients were almost

incapable of fending for themselves, some being unemployable. (3) Immature, 8 cases; these patients showed social irresponsibility and childish traits, were unwilling to face adult responsibility, and were emotionally fickle and unpredictable. (4) Psychoneurotic, 2 cases; alcoholism in these patients appeared to be related to an anxiety state. (5) Not known, 2 cases; these patients showed signs of a mild Korsakoff syndrome.

It is concluded that generalizations cannot be made concerning the highly complex problem of the aetiology of chronic alcoholism into which so many factors, psychiatric, social, and probably occupational, enter. Probably unfavourable circumstances in childhood, such as the influence of unkind, neglectful, over-strict, or hard-drinking parents, may play a part, while in later life an unsatisfactory marriage with a lack of other outlets of emotion or interest may lead to excessive drinking as an easy way of escape. *Myra Mackenzie*

1314. **Studies in Chronic Alcoholism: III. Laboratory Studies**

E. S. FINCKH, B. G. DALE, R. A. JOSKE, and E. G. SAINT. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 738–742, May 31, 1952. 3 figs., 12 refs.

For purposes of diagnosis and clinical assessment radiological, biochemical, and histological studies were made of the stomach, liver, and peripheral nerves in 78 cases of chronic alcoholism (see Abstract 1312). Barium-meal examination of 23 patients revealed no abnormality in 17, gastric ulcer in 3, duodenal ulcer in 2, and oesophageal diverticulum in one. Of the 17 patients with normal radiological findings, 9 had had haematemesis and 7 persistent vomiting or upper abdominal pain, while 7 were shown to have histamine-fast achlorhydria. All 3 patients with gastric ulcer had had haematemesis and melaena, and one, in whom the presence of an ulcer was confirmed by gastroscopy, had histamine-fast achlorhydria. Histamine test-meal examination in 74 patients within a few days of admission showed a maximum acidity of over 60 units of free hydrochloric acid in 12 and of less than 20 units in 33, 18 being found to have achlorhydria. Gastric biopsy was performed on 38 patients and showed normal mucosa in 21 and superficial and atrophic gastritis in the remainder. Biochemical and histological investigations of the liver gave frequent evidence of hepatitis, the histological picture varying from reversible fatty change to a considerable degree of fibrosis which varied little with treatment. Of 43 patients subjected to liver biopsy the findings were normal in 5 and showed only fatty change in 14; in 22 cases fatty change with increased fibrous tissue occurred, and in 2 cases fibrosis without fatty change. These findings seemed to support the opinion that in chronic alcoholism with prolonged malnutrition an initial stage of fatty accumulation is followed by a portal type of cirrhosis, often indistinguishable from that caused by other factors. When peripheral neuritis was present biopsy showed demyelination of the peripheral nerves. Considerable reduction in the signs and symptoms of neuritis followed treatment, but to what extent demyelination is reversible is not known. Post-mortem examination was performed in 12 cases, the most significant findings being hepatic cirrhosis and its complications, encephalopathy, and infections. The changes observed, it is suggested, are mainly caused by malnutrition. *Myra Mackenzie*

1315. **Studies in Chronic Alcoholism: IV. Treatment and Management**

E. G. SAINT, R. A. JOSKE, M. A. MACKAY, and C. N. TURNER. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 742–746, May 31, 1952. 5 refs.

The authors suggest that chronic alcoholism is a more common cause of physical and mental disablement than is generally recognized. Hospital treatment is a necessity to begin with in every case, and as almost every patient is suffering from malnutrition to a great or lesser degree he should be given a well-balanced and nutritious hospital diet, including generous amounts of protein and vitamins, especially the vitamin-B complex. In cases of nutritional hepatitis foods rich in lipotropic factors are needed, and in addition to the normal ward diet, which should contain at least 80 g. of protein, one pint (568 ml.) of milk fortified by the addition of 4 oz. (124 g.) of skimmed milk powder, 1 oz. (31 g.) of lactose, and vitamins should be given daily, providing 140 g. of protein and adequate daily amounts of choline and methionine. Jaundice, recurrent ascites, and massive gastro-intestinal haemorrhage are necessarily of very grave significance, but incipient liver failure has been successfully treated by intravenous administration of 10% glucose solution, serum, and protein hydrolysates, and by intragastric drip feeding with a milk mixture through a Rehfuss tube passed intranasally into the stomach.

The maintenance of good nutrition in alcoholic patients is stressed as all-important, preventing deterioration even if drinking is continued. Follow-up management is a specialized task which needs co-operation between physicians, psychiatrists, dieticians, and social workers. For apparently incurable alcohol addicts institutional care is recommended and a more enlightened approach to the problem is urged. The authors' experience with "antabuse" has been disappointing, though some patients have benefited greatly from its use. *Myra Mackenzie*

TREATMENT

1316. **Probability of Relapse in Dementia Praecox**

L. DANZIGER. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **13**, 111–116, April, 1952. 2 figs., 3 refs.

In a previous study by the author (*Dis. nerv. Syst.*, 1946, **7**, 357) the probability of recovery from dementia praecox after symptomatic treatment was found to follow a simple "decay law". Using similar methods he has now made an attempt to estimate the ultimate prognosis after insulin and electric convulsion therapy (E.C.T.).

The incidence of relapse in patients discharged from New York State Hospitals was calculated, and the figures compared with those based on the theoretical expectation of return to hospital. Agreement between

actual and theoretical values was said to be " fair ". It could be concluded that if on the day of discharge from hospital the patient had recovered after E.C.T., the chances of his returning to hospital eventually were 45 in 100; after insulin coma therapy, regardless of the patient's condition on the day of discharge, the chances of relapse were 55 in 100. It is emphasized that these figures apply only to groups of patients. In both types of treatment the results indicated that a 5-year cure was, for practical purposes, a complete cure, and that after that time the chance of relapse was no greater than the incidence in the general population.

[It seems doubtful if such definite conclusions are justifiable on the data used as the basis of the argument.]

W. T. McClatchey

1317. **Effect of Glutamic Acid on Chronic Psychotic Patients**

W. J. PILE. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **13**, 106–110, April, 1952. 16 refs.

Ten psychotic patients were given 24 g. of glutamic acid divided in 3 doses daily for a period of 6 months; 10 similar patients were given placebos over the same period. Psychological and clinical assessments indicated that glutamic acid had no effect on the patients tested.

W. T. McClatchey

1318. **Follow-up Results in 95 Women Sterilized for Psychiatric Reasons.** (Nachuntersuchungen bei 95 auf Grund psychiatrischer Indikation sterilisierten Frauen)

A. HOLENSTEIN. *Praxis* [*Praxis*] **41**, 413–419, May 15, 1952. 9 refs.

In this paper are reported the results of a follow-up study of 95 women who were sterilized on psychiatric grounds. The women expressed dissatisfaction with the operation for the following reasons: the presence of menstrual disorders (7%); desire for more children (55%); feelings of guilt on moral and religious grounds (5%); psychosomatic disorders (30%). Only 9 women out of the total of 95, however, wholly regretted having had the operation.

Symptoms were most severe when the operation had been performed because of the husband's behaviour (for example, alcoholism), or when it was performed at the wish of some person other than the woman herself, or when the woman had strong maternal feelings and only a small number of children. The author advises that the following conditions should be taken into account before sterilization is performed: the psychiatric condition of the patient; the number of children she already has; her age, religion, and marital and social relationships; and the patient's personality in general. In this series the good effects of sterilization on the whole outweighed the bad, especially where fear of pregnancy marred family relations and was harmful to health. The author further recommends follow-up visits to the doctor after the operation, as counsel and advice on any problems subsequently arising may be a means of avoiding many of the worries which beset this type of patient. [The findings in this study agree in general with those of other investigators.]

N. A. Standen

1319. **Nicotinic Acid Therapy in Psychoses of Senility**

I. GREGORY. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **108**, 888–895, June, 1952. 21 refs.

In a series of 45 patients suffering from " confusional psychoses of senility " treated at the Hollywood Sanitarium, New Westminster, British Columbia, the author has attempted to determine the proportion responding to the administration of nicotinic acid and the degree of their improvement. The patients' condition before and after treatment was assessed clinically and psychometrically (Shipley–Hartford scale). Each received 300 mg. of nicotinic acid 3 times daily by mouth and 100 mg. daily by injection. This dosage was continued for 3 months or until improvement occurred, in which case it was reduced progressively to 100 mg. daily by mouth, which was maintained indefinitely.

Of 14 patients under the age of 65, 8 were considered to show marked improvement, whereas of 31 patients over 65, only 4 improved significantly. Of the 12 patients successfully treated, 3 were under 60, their ages being 55, 57, and 58 years respectively; several were depressed, 3 had had cerebrovascular accidents, in 2 the blood urea level was raised, and in one the blood bromide level was 100 mg. per 100 ml. All showed evidence of arteriosclerosis. After their discharge from hospital, patients were followed up for periods varying from 3 to 15 months. It is concluded that nicotinic acid therapy for the psychoses of senility will give the best results in patients under 65 whose illness is of sudden onset and short duration.

[The diagnoses made in these cases are questionable, while the author's assumption that the coincidence of administration of nicotinic acid and improvement proved the interdependence of the two events shows considerable naïvety. The view that senescence begins at 55 will not receive general acceptance.]

L. G. Kiloh

1320. **Use of Dehydro*iso*androsterone in Psychiatric Treatment. A Preliminary Survey**

E. B. STRAUSS, D. E. SANDS, A. M. ROBINSON, W. J. TINDALL, and W. A. H. STEVENSON. *British Medical Journal* [*Brit. med. J.*] **2**, 64–66, July 12, 1952. 2 refs.

In view of the reported relationship between abnormal steroid excretion and abnormal mental states the authors have investigated the effect of dehydro*iso*androsterone on constitutionally immature patients suffering from mild schizophrenia and " schizoid psychopathy " who also showed quantitative abnormalities in the excretion of 17-ketosteroids. At St. Bartholomew's Hospital, London, and St. Ebba's Hospital, Epsom, 8 male patients whose ages ranged from 17 to 33 received intramuscular injections of 5 to 50 mg. of dehydro*iso*androsterone every day or every second day for periods of several weeks. During and after the treatment most of the patients felt more energetic and confident, and it was observed that they became more alert and virile. On the other hand 2 patients became so paranoid and aggressive that the injections had to be stopped.

From a preliminary trial the authors are satisfied that the drug increases self-confidence and induces euphoria, but they believe that more study will be required to

determine whether these changes are related to alterations in 17-ketosteroid excretion. They suggest that " the beta fraction of the 17-ketosteroids represents the metabolites of substances which may be concerned with the development of ' self-confidence ' in adolescence or early adult life ". *Hunter Gillies*

1321. **Treatment of Inadequate Personality in Juveniles by Dehydro*iso*androsterone. Preliminary Report**
D. E. SANDS and G. H. A. CHAMBERLAIN. *British Medical Journal* [*Brit. med. J.*] **2**, 66–68, July 12, 1952. 1 ref.

Proceeding from the work of Strauss *et al.* (see Abstract 1320) the authors have studied the effects of dehydro*iso*androsterone on 2 groups of male patients aged 12 to 18 at St. Ebba's Hospital, Epsom. The first group consisted of 13 boys who were constitutionally and emotionally immature and inadequate, and the second of 4 boys known to have " aggressive trends ". Although they were selected for treatment on clinical grounds, the excretion of 17-ketosteroids was estimated in all but one of the patients: it was found to be normal in half the cases and reduced in the remainder. The drug was given in doses ranging from 10 mg. twice weekly up to 40 mg. daily, its effects being the same whether it was given by mouth or by intramuscular injection. Within 4 days to 4 weeks of starting treatment all the boys in the first group became more active, forthcoming, and confident, and more heterosexual. No physical change or maturation was observed, but in every case weight increased or was maintained. In the second group a marked increase in aggressiveness occurred in all cases soon after starting treatment.

The effects produced were temporary in both groups, the patients reverting to their previous condition when administration of the drug was stopped. It is therefore suggested that in cases of inadequate personality the treatment replaces certain factors essential for " normal constitutional endowment " and, although providing no substitute for psychotherapy, may enable progress to be accelerated through improved rapport and increased self-confidence.

[Although, as in the series reported by Strauss *et al.* (see Abstract 1320), the effects of suggestion were not ruled out by treating a control series with inert injections, and although the drug may well have acted as a simple euphoriant, the results are promising and the work merits continuance.] *Hunter Gillies*

1322. **Procaine Block of Frontal Lobe White Fibers as a Means of Predicting the Effect of Prefrontal Lobotomy. I. Experimental Studies**
O. T. BAILEY, W. T. SMALL, and F. D. INGRAHAM. *Journal of Neurosurgery* [*J. Neurosurg.*] **9**, 21–29, Jan., 1952. 6 figs., 4 refs.

The authors have carried out experiments aimed at predicting in some measure the result of division of the white fibres in the frontal lobe of the brain by procaine block of those fibres. As a preliminary to clinical trials 1 or 2% procaine hydrochloride was injected into the frontal white fibres of cats, which were then killed at varying intervals. The extent of procaine spread was determined by a modification of the colour-reaction method of Riegel and Williams in which 2-mm. slices from the frozen brain were exposed first to nitrous acid vapour and then to ammonia, a yellow-orange colour being obtained if there was a concentration of procaine of 0·00045 mg. or more per ml.

The authors found that there was very little evidence of local diffusion of procaine, and in less than an hour there was not a sufficient concentration left to give a positive colour reaction. The results of histological examination carried out 1 hour and again 1 month and 2 months after injection were almost identical quantitatively and qualitatively with those obtained after injection of an equal quantity of normal saline. No objectionable general reactions were observed unless procaine was allowed to enter the subarachnoid space or the ventricular system, in which case the animal died immediately. This could be prevented by careful technique.

These findings indicated that the procedure could be applied to human patients with reasonable assurance of its safety. *W. McAdam*

1323. **Procaine Block of Frontal White Fibers as a Means of Predicting the Effect of Prefrontal Lobotomy. II. Clinical Evaluation**
W. P. VAN WAGENEN and C. T. LIU. *Journal of Neurosurgery* [*J. Neurosurg.*] **9**, 30–51, Jan., 1952. 1 ref.

Procaine was injected by various techniques into the frontal-lobe white fibres of 20 psychotic and 6 non-psychotic patients. In one technique, which is described, burr holes were made either over the frontal poles or just anterior to the coronal suture, and the pia and arachnoid sealed to the brain by means of the coagulating current; after two days 3 ml. of 2% procaine was injected on each side. In 23 of the 26 patients leucotomy was later performed. In 10 cases the patient's condition was improved by the block and later also by leucotomy; in 7 neither procedure caused any improvement; and in 6 the results were equivocal.

[Lindsay (*J. ment. Sci.*, 1950, **96**, 923) has described the results of a similar procedure in 3 patients on whom leucotomy was performed. He suggested that the method might be of value in forecasting the results of a second operation, but no such trials were described. In the present study the effects of procaine block and leucotomy corresponded in about two-thirds of the cases. While it is possible that with further study and more precise technique of operation the method might be of value, anatomical considerations suggest that this is the best that can be expected of any " blind " approach; and clinical assessment can now be at least as accurate.]
W. McAdam

1324. **Clinical and Electroencephalographic Effects of Prefrontal Lobotomy and Topectomy in Chronic Psychosis**
E. G. KRUEGER and H. L. WAYNE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **67**, 661–671, May, 1952. 4 figs., 26 refs.

Dermatology

1325. **Thiopentone Narcosis in Dermatology.** (L'emploi de la narcose sous pentothal en dermatologie)
S. LAMBERGEON. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **79**, 20–24, Jan.–Feb., 1952. 15 refs.

Thiopentone narcosis may be helpful in the diagnosis and psychotherapy of psychosomatic dermatological disorders, and the drug may also be of therapeutic value simply through its anaesthetic effect. Thus pathomimia was suppressed in several cases treated by the author, and in about 20 cases improvement resulted from the release of underlying emotional tension. In one case of residual pruritus a cure was achieved by simple anaesthetic action. The contraindications and risks are detailed. *James Marshall*

1326. **The Clinical Evaluation of a New Synthetic Antihistaminic Preparation.** (Valutazione clinica di un nuovo preparato antiistaminico di sintesi)
L. LEVI and L. DATOVO. *Giornale Italiano di Dermatologia e Sifilologia* [*G. ital. Derm. Sif.*] **93**, 79–87, Jan.–Feb., 1952. 6 refs.

A combination of "antistin" and "pyribenzamine" was given in a dosage of 150 mg. 3 times a day for 10 days in the treatment of itching allergic dermatoses. In 14 of the 21 patients treated the response was rapid and favourable, in 4 it was less so, and in 3 the treatment appeared to be ineffective. Itching was relieved first and healing of the lesions followed. An intramuscular injection in 17 patients of 1 mg. of histamine before and after treatment showed that the drugs reduced, but did not abolish, the hypotensive and cardiac accelerator effects of the histamine. The weal produced by intradermal injection of histamine solution was also lessened by treatment with this mixture, which is considered to exert its beneficial effect in dermatoses partly by a direct antihistaminic action and partly by a sedative effect on the autonomic nervous system. *James D. P. Graham*

1327. **Norwegian Scabies**
G. C. WELLS. *British Medical Journal* [*Brit. med. J.*] **1**, 18–20, July 5, 1952. 17 refs.

An epidemic of 67 cases of Norwegian scabies originating at University College Hospital, and spreading by transfer of a patient to St. Pancras Hospital, London, is described. The infection was traced back to a woman of 67 who had been admitted with a widespread scaling dermatosis which had started 2 years before with blisters and cracks on the hands. She had been in contact with scabies 3 or 4 years previously, but had had no treatment. The patient was emaciated and had deformities of the limbs resulting from rheumatoid arthritis in the past. There was profuse scaling of the lower part of the trunk, sparse hair, and scaling of the scalp, neck, and ears, with dry crusting of the hands. She was depressed and complained of generalized itching. The correct diagnosis was not made until the epidemic broke out and a search for a scabies carrier was made. It was then found that scales from all parts of the body were swarming with mites, eggs, larvae, and nymphs, which were morphologically indistinguishable from *Sarcoptes scabiei* var. *hominis*.

In the contact cases it was rare to find typical scabies burrows or lesions on the wrists or fingers, and a difference in distribution of the lesions was noted between nurses and patients in that the former showed most lesions on the arms, while the latter were affected on the waist, buttocks, and thighs. Many of the patients had not had direct contact with the source of infection and it seemed probable that the infection was transferred on the nurses' arms from patient to patient.

The author reviews the literature on Norwegian scabies and comments on the fact that the condition, which is a variant of ordinary scabies, is almost unknown in the physically and mentally normal. It is suggested that where scratching is reduced in the absence of itching or for other reasons in cases of chronic physical or mental disease, there may be unrestricted multiplication of the mites in the horny layer of the skin, and that this may lead to a temporary change in biological habit so that the female no longer forms a discrete burrow.
Benjamin Schwartz

1328. **Two Cases of Vacciniform or Varicelliform Cutaneous Diphtheria.** (Deux nouveaux cas de diphtérie cutanée vacciniforme ou varicelliforme)
P. LE COULANT and —. SOURREIL. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **79**, 48–53, Jan.–Feb., 1952. 3 figs.

A description is given of 2 further cases of varicelliform or vacciniform cutaneous diphtheria (proved bacteriologically) in infants of 6 and 8 months respectively, one of whom died, in addition to the 5 such cases previously described by the same authors (*Ann. Derm. Syph., Paris*, 1951, **78**, 300; *Abstracts of World Medicine*, 1951, **10**, 435). This variety of cutaneous diphtheria is not sufficiently well recognized, and may account for some cases of Kaposi's varicelliform eruption. *James Marshall*

1329. **A Clinical Report on the Treatment of Contact Dermatitis with Adrenocorticotropic Hormone in Oil**
L. N. GAY and G. W. MURGATROYD. *Journal of Allergy* [*J. Allergy*] **23**, 215–221, May, 1952. 2 refs.

Four patients who developed dermatitis after the use of a medicated ointment and 4 others with dermatitis after contact with poison ivy were given corticotrophin (ACTH) in oil in one injection daily, the single dosage ranging from 40 mg. to 160 mg., the total from 60 to 420 mg. Recovery was complete in 2 to 6 days.
H. Herxheimer

Paediatrics

Correction.—In Abstract 994 in the September issue, on "The Aetiology of Retrolental Fibroplasia", *for* "carbon dioxide" *read* "oxygen" throughout.

1330. **Bronchiectasis in Infancy.** (Algunas consideraciones sobre las bronquiectasias en la infancia)
L. LOPEZ AREAL. *Revista Española de Tuberculosis* [*Rev. esp. Tuberc.*] **21**, 125–146, March, 1952. 13 figs., bibliography.

The author, Director of the Bilbao Sanatorium for Children, discusses the features of bronchiectasis in infancy, and points out that there has been no real improvement in the treatment of the disease since he last wrote about it in 1944. It is still frequently misdiagnosed. He describes 21 cases in detail, of which one-third were admitted to hospital as cases of tuberculosis, although with a negative tuberculin reaction. He believes that surgery is the only treatment of permanent value when there is bronchial dilatation, but was able to have only one of his patients operated upon, with a good result. He considers the incidence to be at least 21 per 1,000 children in sanatoria. In virtually all cases the condition is acquired. In the 21 cases, bronchiectasis followed tuberculosis in 7 cases, pneumonia or whooping-cough in 10, and only in 4 did there not appear to be a definite causative illness. Diagnosis is not difficult: persistent catarrh, profuse sputum, and a radiograph which does not show any signs of tuberculosis should suffice for diagnosis. Bronchography is not necessary for diagnosis, but is essential before any surgery is undertaken. Medical treatment consists largely in the administration of antibiotics and in postural drainage, frequently as the preliminary to surgery at a chosen time.

Since adult bronchiectasis is almost always a process which begins in childhood it is very important that respiratory disease should be carefully and thoroughly treated in the young, since this prophylactic treatment will be far more effective than any later attempts at cure. The author quotes figures, derived from several sources, showing the mortality of bronchiectasis to lie between 25% and 50% of cases, and that the only results which give any hope of reasonable success follow surgery.

J. G. Jamieson

1331. **The Value of Radiology in the Study of Intracranial Haemorrhage and its Sequelae in the Newborn.** (Importanza dell'indagine radiologica nello studio delle emorragie endocraniche del neonato e dei loro esiti)
C. TORRICELLI. *Clinica Pediatrica* [*Clin. pediat., Bologna*] 34, 73–88, Feb., 1952. 12 figs., 27 refs.

The methods in use in the author's paediatric clinic at Milan to solve the diagnostic problems presented by suspected intracranial haemorrhage in the newborn are described. Routine radiography of the skull is first undertaken; if signs of raised intracranial pressure are present in the plain film, the patient is subjected to "pneumoencephalocisternography". The infant is given a sedative on the preceding day, premedicated with morphine, and is anaesthetized with rectal thiopentone. Respiratory arrest sometimes occurs, so that suitable therapy should be at hand. Maximal quantities of cerebrospinal fluid are removed [by lumbar and cisternal routes simultaneously, apparently] and replaced by air. Radiography is undertaken in the conventional positions; information is thus obtained as to the size of the subarachnoid space and ventricles and the presence of obstructions. Carotid angiography is next undertaken, with 5 to 10 ml. of a contrast medium such as "perabrodil". Particular attention is paid to the arterial phase. [Radiographs of 12 cases are reproduced, but no details of results are given.]

Donald McDonald

1332. **Blood Formation in Infancy. Part I. The Normal Bone Marrow**
D. GAIRDNER, J. MARIS, and J. D. ROSCOE. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **27**, 128–133, April, 1952. 2 figs., 19 refs.

At Cambridge Maternity Hospital serial blood and tibial marrow examinations were carried out on 25 infants aged from a few minutes to 3 months. Total cell counts and differential counts of 200 cells were determined on aspirated marrow material. In some cases several sites were punctured and marrow samples compared. There was good qualitative as well as quantitative agreement between them, and this was confirmed on histological examination of sections from material obtained at necropsy on 10 infants who had died soon after birth or were stillborn. The total cell count usually fell from about 136,000 marrow cells per c.mm. at 1 day of age to 35,000 at 10 days of age, and then slowly rose to reach 200,000 at 3 months. These changes were not due merely to dilution of cells with blood. Differential counts and absolute figures showed that the number of immature myeloid cells remained almost unchanged. The concentration of erythroid, myeloid, and lymphoid elements in the marrow aspirate was a good indication of haematopoietic activity. There was an average of about 12% smear cells in the marrow of infants, and these were regarded as lymphocytes. The morphology of cells in infants was identical with that seen in adults. Megaloblasts were not observed.

At birth the marrow contained about 40% of erythroid cells, or about 46,000 per c.mm.; this fell to 8% or 3,000 per c.mm. at 10 days of age, and rose to 15% or 30,000 at the age of 2 months. The reticulocyte count in the marrow gave little additional information as it ran parallel to that in the peripheral blood. The percentage of mitotic figures in early normoblasts reflected

erythroid activity. The myeloid cell count behaved similarly, there being an early fall followed by a slow rise. Lymphoid cells showed a steady slow rise both in percentage and in absolute numbers until they formed 50% of the marrow cells at 4 weeks of age. The presence of many lymphoblasts in the marrow suggested that many lymphocytes are formed in the marrow in infancy. The myeloid : erythroid ratio is of little value in infants.

E. Neumark

1333. **The Blood Picture in Chronic Granulocytopenia in Childhood.** (Das Bild der chronischen Granulocytopenie im Kindesalter)

M. R. VRTILEK. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **7**, 207–228, April, 1952. 7 figs., bibliography.

From the University Children's Clinic, Zürich, the author describes 6 cases of chronic agranulocytosis in infancy and early childhood. Characteristic features were impairment of appetite, failure to gain weight, mild retardation of physical and mental development, and generalized muscular weakness. The general health was usually relatively good, but was broken by frequent intercurrent infections during which moderate enlargement of spleen, liver, and lymph nodes was common. Neutropenia was invariable, but associated lymphocytosis sometimes brought the total leucocyte count to within normal limits and appeared to be a favourable prognostic sign. Moderate anaemia accompanied the disorder in 4 cases, and in 1 case eosinophils were persistently absent from the blood. Hyperplasia of myeloid marrow with immature normoblastic erythropoiesis and reduction in the number of megakaryocytes was usually evident. Only one case proved fatal. Haematinic therapy was without effect in any case, and reliance had to be placed on blood transfusion, with administration of antibiotics to counteract infection.

The differential diagnosis from other forms of agranulocytosis is discussed. The cause of chronic idiopathic agranulocytosis remains obscure, but constitutional weakness of the bone marrow is regarded as probably the fundamental lesion.

Mary D. Smith

NUTRITION AND METABOLISM

1334. **Glycogen Disease**

S. VAN CREVELD. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **27**, 113–120, April, 1952. 3 figs., 25 refs.

The author described his first case of glycogen disease in 1928, a year before the appearance of von Gierke's account of the post-mortem findings. He has followed up the original patient, a boy, from childhood to the age of 30, and in this paper he reports the clinical progress and biochemical changes which have occurred during the period of observation in this case, and also in that of his second patient, a girl of 5 who has now reached the age of 24.

Both the patients are mentally and physically normal adults. The boy's epiphyses were late in uniting and his second dentition was delayed, but subsequent development was normal and he is married and has a son. The girl's second dentition and puberty occurred at the normal ages. She is married and has had one pregnancy which ended in abortion. There was a gradual decrease in the size of the liver after puberty, with a corresponding diminution of abdominal protuberance, and the liver in both cases is now only just palpable. The fasting blood sugar concentration increased over the years to normal levels and ketonuria ceased to occur in the fasting state. Some defect in the mobilization of glycogen has, however, persisted: injections of adrenaline still fail to produce an increase in the sugar and lactic acid content of the blood. The blood cholesterol level, raised in the early stages of the disease, later became normal.

The author also surveys the early history of glycogen disease and discusses the differential diagnosis of hepatomegalia glycogenica and cardiomegalia glycogenica, the aetiology (with mention of the possible role of corticotrophin), and the treatment.

K. Black

1335. **Effects of Early Feeding of Strained Meat to Prematurely Born Infants**

M. B. ANDELMAN, P. S. GERALD, A. C. RAMBAR, and B. M. KAGAN. *Pediatrics* [*Pediatrics*] **9**, 485–491, April, 1952. 6 refs.

This study was undertaken to determine the effect on prematurely born infants of the feeding of strained meat. One group of infants received a standard formula; another an identical formula to which strained meat was added; and a third group was breast fed.

Meat added to the diet of prematurely born infants weighing between 2,000 and 6,750 g. was well accepted. There was no significant difference in the symptoms or signs of illness among the infants of either of the three groups. It was found that a plot of the body weight of such infants against age generally gives a smooth sigmoid curve. The central portion of the " S " forms a remarkably straight line. The linear portion of the curve is located in the interval between 2,500 and 4,500 g. body weight. The location is relatively unaffected by either age or birth weight. The slope of this linear portion was taken as the measure of the weight gain. A similar relationship was found for the crown–heel length. These findings are not only of academic interest but are also of practical importance since they provide an unusually good tool for further nutritional and other studies.

Growth as measured by rate of change of weight and length did not differ significantly between the experimental group and the control group. The breast-fed group exceeded the experimental and control groups in both weight and length gain. The greater weight gain in the breast-fed group as compared to the experimental group was statistically significant.

Minimum values for red blood cell count and haemoglobin were observed at 12 weeks of age. These values rose steadily until about 20 weeks of age, at which time they became relatively stable. There was no significant difference in the haemoglobin concentration or red blood cell count between the three groups at 12 weeks of age. At 20 weeks, however, the meat-fed or experimental

group exceeded the control by a significant amount. The mean difference in haemoglobin concentration of the experimental group and that of the control group was 1·0 g./100 cc. This finding is of interest, especially since the experimental and control groups both received more than adequate amounts of iron added to the diet.

A gradual rise in serum protein concentration was noted with increasing age. At 12 weeks of age, the serum protein concentration for the breast-fed group was significantly lower than that for the experimental group, the average difference being 0·40 g./100 cc. The average difference between these two groups at 20 weeks was 0·35 g./100 cc. but there were too few in the breast-fed group at this time to give the difference statistical significance. The serum protein concentrations in the experimental and the control groups did not differ significantly at either 12 or 20 weeks of age.

Analysis of the total volume intake of the formulae showed that intake of the experimental group was reduced in proportion to the greater caloric content of the meat-containing formula. The result was that the daily intake of calories was the same in both the experimental group and the control group. This remarkable reduction in volume of intake by premature infants in the weight groups concerned and the strikingly uniform caloric intake are of interest particularly in view of current thoughts on self selection of diet.

No differences were noted in the weight or length gain, haemoglobin, red blood cell count, or serum protein concentration between the experimental group and the control group when the infants reached one year of age. —[Authors' summary.]

1336. **The Vitamin B Complex as a Supplement in Infant Feeding**

J. A. CHALMERS. *Edinburgh Medical Journal* [*Edinb. med. J.*] **59**, 247–254, May, 1952. 36 refs.

There is suggestive theoretical evidence, which is reviewed by the author, that both human and cow's milk may be deficient in the vitamin-B complex in relation to the needs of the infant. To examine the practical implications of this theory, 188 newborn infants, of whom over half were artificially fed on half-cream dried milk, were given a vitamin-B supplement which supplied 500 mg. of aneurin, 1,000 mg. of riboflavin, and 5,000 mg. of nicotinamide daily and compared with a control group of 192 infants.

The length of stay in hospital, the weight gain or loss, and the rate of regain of birth weight were not significantly different in the two groups. The explanation offered for the failure in this study to demonstrate the spectacular effect of vitamin B reported by certain other workers is that there is an adequacy of vitamin-B complex in the maternal diets of the population studied, with good storage by the foetus. *David Morris*

1337. **On the Peptic Digestibility of Some Infant Milks and Milk Mixtures *in vitro*.** [In English]

H. KALLIALA. *Annales Medicinae Experimentalis et Biologiae Fenniae* [*Ann. Med. exp. Biol. Fenn.*] **30**, Suppl. 1, 1–67, 1952. 8 figs., bibliography.

1338. **The Absorption of Vitamin A Administered per Rectum.** (Sull'assorbimento della vitamina "A" per via rettale)

L. BARILLI and P. PERUZZI. *Rivista di Clinica Pediatrica* [*Riv. Clin. pediat.*] **50**, 196–199, March, 1952. 1 fig., 5 refs.

In an attempt to assess the absorption of vitamin A by the rectal route the authors administered it in suppositories in amounts calculated to supply 2,000 to 7,500 i.u. of the vitamin per kg. body weight to a group of 10 children aged 11 months to 10 years. In blood samples taken at 30, 60, and 120 minutes they found a rapid rise in blood levels of the vitamin of the order of 350 i.u. per 100 ml. over the first hour, followed by an equally rapid fall to pre-treatment levels. They conclude that the coefficient of utilization by this route is adequate, and that the rapidity of absorption is second only to that of intravenous administration, and point out the obvious advantages of the rectal route in children. *A. Paton*

CARDIOVASCULAR SYSTEM

1339. **Paroxysmal Tachycardia in Infants and Children. Study of 41 Cases**

A. S. NADAS, C. W. DAESCHNER, A. ROTH, and S. L. BLUMENTHAL. *Pediatrics* [*Pediatrics*] **9**, 167–181, Feb., 1952. 14 figs., 22 refs.

This study of the aetiology, electrocardiographic features, and prognosis of paroxysmal tachycardia in infants and children is based on 41 such cases seen during the past 20 years at the Boston Children's Hospital. In 24 cases (including 4 cases of Wolff–Parkinson–White syndrome) no aetiological factors could be recognized. Of the remaining 17 patients, 8 had congenital heart disease. The age at onset was 4 months or less in 24 cases, and ranged from 7 months to 13 years in the other 17 cases, a greater proportion of idiopathic cases occurring in the former group and all but one being in males. Of the total of 41 patients, 31 were male. The majority of the patients were very ill, ashen grey, perspiring, restless, and irritable, with rapid, laboured respiration, a hacking cough, and a distended abdomen; the clinical picture was very like that of pneumonia except for the excessively frequent pulse. Other signs were enlargement of the heart, vomiting, pulmonary congestion, oliguria, peripheral oedema, and fever. Signs of cardiac failure were present in 22 cases. Unlike adults, children with paroxysmal tachycardia tend to develop congestive failure, but do not usually complain of either pain or palpitations.

Laboratory tests were negative. Radiological examination showed enlargement of both ventricles and often of the right atrium, with pulmonary vascular congestion. Failure was more likely with pulse rates over 180 per minute, when attacks persisted for more than 24 hours, and in the younger age group. Electrocardiographic changes, absent between attacks, are described in detail. There was supraventricular tachycardia in 29 cases, paroxysmal auricular flutter in 9, and ventricular tachycardia in 3.

The attacks ended spontaneously in 6 cases. Reflex vagal stimulation succeeded in only one of 17 cases so treated. For supraventricular tachycardia and auricular flutter the administration of digitalis is recommended, the digitalizing dose being 1·0 to 1·2 mg. of digitoxin or its equivalent per square metre of body surface, or 0·04 to 0·06 mg. per kg. body weight, given in 3 doses within 16 or 24 hours; this is followed by a daily maintenance dose of one-tenth the digitalizing dose for at least one week. Oxygen was valuable in the attacks, and antibiotics are now usually given. The use of quinidine is advised for ventricular tachycardia, but the authors consider that procaine derivatives may also prove useful. A continued maintenance dose of quinidine may diminish the frequency of recurrences of the Wolff–Parkinson–White syndrome and ventricular tachycardia. The authors are uncertain whether drugs affect recurrences in other types.

Of the 41 patients studied, 3 died in an attack, 2 died from unrelated causes, and 31 survived for periods of 1 to 20 years. Of these last, 8 had only one attack, but 13 have had innumerable attacks. Infants, unlike the older children, do not have recurrences after the first year.

A. W. Franklin

GASTROENTEROLOGY

1340. **Duplications of the Alimentary Tract**
R. E. Gross, G. W. Holcomb, and S. Farber. *Pediatrics* [*Pediatrics*] **9**, 449–468, April, 1952. 17 figs., 11 refs.

Duplications of the alimentary tract are defined by the authors as " spherical or tubular structures possessing a well-developed smooth muscle layer and lined with a mucous membrane. . . . They are found at any level from tongue to anus and are usually attached to some portion of the alimentary tube ". The authors discuss the embryology of these duplications, and analyse their findings in 68 cases seen at the Children's Hospital, Boston.

The duplications found in these cases were situated as follows: at the base of the tongue (1 case); within the thorax (13 cases); arising in the abdomen but passing into the thorax (3 cases); attached to the stomach (2 cases), to the duodenum (4 cases), to the jejunum (4 cases), and to the ileum (20 cases); in the ileocaecal area (8 cases); attached to the caecum (3 cases), to the transverse mesocolon (1 case), or to the sigmoid colon (2 cases); and posterior to the rectum (3 cases); there were 4 double lesions of the colon and rectum. With one exception all the duplications of the small intestine were found along the mesenteric border. The commonest type was a spherical structure varying in diameter from 1 to 10 cm. and attached to some part of the intestine; less often it was a tubular structure as much as 65 cm. in length and occasionally so incorporated in the intestinal or colonic wall that no abnormality was suspected. The rarest type was a round, cystic structure lying free in the peritoneum except for a thin mesenteric stalk.

Microscopically, the duplication showed a marked resemblance to normal intestine, having a mucous membrane (not necessarily similar in type to that of the adjoining alimentary tract), one or more muscle layers, and often a serosal coat. The mucous membrane was sometimes destroyed by peptic digestion or, in the cystic type, by excessive internal pressure. When the duplication was closely attached to the intestine there was frequently a common wall and a common musculature. The duplication usually contained a clear, colourless, mucoid fluid, but when peptic digestion or excessive pressure had occurred the fluid was haemorrhagic or dark. If the duplication was connected with the normal intestine its contents resembled those found in that particular part of the intestine.

The clinical manifestations were usually due to pressure of the tumour on the adjoining intestine, leading to partial obstruction; in some cases there were pain and haemorrhage from ulceration, while in some cases the condition was found by chance on routine radiography.

Early surgical treatment is advised. Where the duplication adheres closely to the normal intestine and there is no line of cleavage between the two, removal of part of the normal intestine is necessary; on the other hand in many cases of duplication of the rectum or colon the double lumen may be left, only the lower end of the anomaly, where trouble usually arises from an additional or imperforate anus or from communication with other organs, needing attention. Marsupialization is not advocated.

H. G. Farquhar

1341. **The Use of Banthine Bromide in Infantile Colic and Vomiting. Preliminary Report of Fifty Cases**
H. Levy and B. M. Sweifler. *Journal of Pediatrics* [*J. Pediat.*] **40**, 570–575, May, 1952. 32 refs.

At the Beth-El Hospital, Brooklyn, N.Y., " banthine " bromide was given to 50 infants ranging in age from 1 to 32 weeks, 25 of them being between 1 and 4 weeks of age. They were divided into three groups according to the most troublesome symptom; 23 infants had colic only, 12 had vomiting, and 15 had both colic and vomiting. A detailed analysis of the 50 cases is presented in a table. The drug was usually given in 5-mg. doses 4 times a day, and with this dose no toxic effects were observed. Two infants had marked flushing with single doses of 10 mg., but 5 others received total daily doses of 30 mg. without any toxic manifestations.

The results were as follows: good, 34; moderately good, 6; and poor, 10. Usually a good result occurred within 24 to 48 hours and was most dramatic in the cases of vomiting and of colic with vomiting. Of the 8 patients who had been given other drugs without improvement, in 7 the results of treatment with banthine were good and in 1 poor. Although definite conclusions are not justified in a comparatively small series such as this, the authors believe that banthine bromide has a place in the symptomatic treatment of infantile colic and vomiting or possibly even as a curative agent. Further investigations are in progress to explore the usefulness of banthine in paediatric practice, particularly in cases of pylorospasm.

B. S. P. Gurney

Public Health

1342. **The Use of Triethylene Glycol Vapor for Control of Acute Respiratory Diseases in Navy Recruits.—I. Physical Factors and the Effect of Air-borne Bacteria**
UNITED STATES NAVAL MEDICAL RESEARCH UNIT NO. 4. *American Journal of Hygiene* [*Amer. J. Hyg.*] **55**, 203–214, March, 1952. 3 figs., 21 refs.

Triethylene glycol (TEG) was vaporized in dormitories in 2 barracks for U.S. Naval recruits. Each barrack contained 4 dormitories arranged in pairs, the TEG being vaporized in the lower room in 3 cases, while in one pair water was vaporized as a control. The concentration of TEG in the lower dormitory was usually above 2·5 μg. per litre of air, but was less than this in the upper dormitory. For bactericidal and virucidal action of TEG there is an optimum range of relative humidity and temperature, and this was mostly achieved. A rough visual estimation of TEG concentration based on fog density proved reasonably accurate and, if anything, tended to err on the low side. Despite occasional heavy fog, no condensation of TEG was detected and there were no complaints from the recruits in the barracks.

A 65% reduction in air-borne bacteria in the dormitories where TEG was vaporized was achieved and a smaller percentage in the dormitories immediately above. Oiling of the floors caused a reduction in both the control and test dormitories, but the relative reduction in the dormitory where TEG was vaporized persisted. The combination of TEG vapour and oiled floors, however, did not prevent streptococci from settling on plates 5 feet (1·5 m.) above floor level. Bacterial samples were taken with calibrated Folin bubbler samplers; 1 cubic foot (0·028 cu.m.) of air per minute was bubbled through nutrient broth containing a few drops of olive oil as an anti-foam agent.

Ronald S. McNeill

1343. **The Use of Triethylene Glycol Vapor for Control of Acute Respiratory Diseases in Navy Recruits.—II. Effect on Acute Respiratory Diseases**
UNITED STATES NAVAL MEDICAL RESEARCH UNIT NO. 4. *American Journal of Hygiene* [*Amer. J. Hyg.*] **55**, 215–229, March, 1952. 2 figs., 15 refs.

The effect of triethylene glycol vapour (see Abstract 1342) on the incidence of acute respiratory diseases in naval recruits living in barracks was studied from September, 1950, to April, 1951, the number of men being 1,375. The men entered the barracks for a training period of 9 to 11 weeks, and equal numbers were assigned to dormitories treated with TEG vapour and to control dormitories at the other end of the barracks.

The test and control groups were comparable as regards age, history of infectious diseases and tonsillectomy, and the district from which they came. Each man was examined clinically every week and blood specimens were collected at the first, at an interim, and at the final examination. Nose and throat cultures were also taken from all recruits attending the infirmary for respiratory disease. β-Haemolytic streptococci were isolated and typed, and haemagglutination titres for influenza and antistreptolysin-O titres were determined. Influenza was diagnosed on a fourfold rise in haemagglutination titre; a streptococcal infection was diagnosed if Group A streptococci were isolated in the presence of exudative tonsillitis or if there was a rise in antistreptolysin-O titre. Respiratory infection of unknown aetiology formed the remaining group, and included common colds, rhinitis, bronchitis, and pharyngitis.

The results show that epidemics of influenza and of streptococcal and other respiratory infections occurred in both the treated and control dormitories, the total number of infections in each group being approximately equal, with only 3% of the men escaping infection completely. The behaviour of acute respiratory disease was not modified, therefore, by TEG vapour in dormitories. It is pointed out, however, that recruits spend only 60% of their time in barracks, and ample opportunity exists in class-rooms and in the mess for contact spread within and between companies. The limitation of the vapour to the barracks only may have been the reason for its failure.

Ronald S. McNeill

1344. **An Epidemiological Study of Bornholm Disease.** (Epidemiologische gegevens over de Bornholmse ziekte)
L. F. SCHAEFFER. *Nederlandsch Tijdschrift voor Geneeskunde* [*Ned. Tijdschr. Geneesk.*] **96**, 1200–1207, May 17, 1952. 4 figs., 2 refs.

In a 12-week epidemic (May to August, 1951) of Bornholm disease affecting a fairly isolated garden suburb near Amsterdam, 429 cases were seen by the author in his practice, which contained about 40% of the total population of 8,754. A high infectivity was indicated by the involvement, in infected families, of about half the members above the age of 15, and of about two-thirds of the younger children. Estimated morbidity rates of 29% for those below the age of 15 and 5·6% for those above signify a predilection for children. The method of spread was mainly through the schools, the disease being introduced by schoolchildren in 66·4% of family infections. Study of spread within the family, particularly to adults, confirmed a common incubation period of about 4 days. That the disease confers some degree of immunity is suggested by the heavier incidence among children and the relatively large number of mild cases in adults. The critical age of 14 might indicate an epidemic about this number of years previously, but this could not be confirmed. There was evidence that infants under 5 months possessed a considerable degree of immunity, but infants over 5 months were often seriously ill. The advent of the school holidays produced a marked fall in the number of new cases.

R. Crawford

Industrial Medicine

1345. **Some Colloidal Properties of Inert Dusts**
R. F. HOUNAM. *Archives of Industrial Hygiene and Occupational Medicine* [*Arch. industr. Hyg. occup. Med.*] **5**, 375–386, April, 1952. 4 figs., 12 refs.

The author puts forward a theory (which he admits has been suggested before) that the apparent solubility of silica and other dusts is due to the presence of finely divided material and is therefore related to the dispersibility of the dust. The dispersibility can be measured directly by preparing suspensions of the dusts and studying their rate of clearing. Alternatively, it may be measured in terms of the " methylene-blue figure ", that is, the amount of methylene blue needed to produce precipitation of a stable suspension of the dust by neutralization of the charges carried by its particles.

Experiments are described in which various dusts and mixtures of dusts were tested in this way, mineral dusts such as silica, alumina, and slate being suspended in water and the carbonaceous dusts such as carbon black, anthracite, and bituminous coal in 50% alcohol, since they are not wetted by pure water. [No details are given of the particle size distributions of the dusts tested, which do not appear to have been determined.]

In a futher discussion of the theory that the solubility of dusts is really a measure of the amount of fine material in suspension, the author recognizes the difficulty of reconciling it with the evidence of King (*Biochem. J.*, 1939, **33**, 944) that the molybdate method of measuring silica solubility is insensitive to particulate silica; nevertheless he claims that " the results of certain experiments are more satisfactorily accounted for by assuming that the very fine silica particles do give a colour reaction with ammonium molybdate ". He then goes on to attempt to correlate his findings with the toxicity of the dusts and suggests that the greater the negative charge carried by the particles, the more toxic the dust, the particles of those dusts which are generally considered harmless being uncharged or carrying a positive charge. In support of this theory he gives methylene-blue figures for silica, anthracite, steam-coal, and bituminous-coal dusts, the last three coming from collieries " where the incidence of pneumoconiosis may be described as high, medium, and low respectively ".

The figures given, interpreted according to the author's theories, suggest that silica and anthracite are of almost equal toxicity, while steam coal is much less toxic and bituminous less still, whereas on the basis of dispersibility, steam-coal dust should be much less toxic than the others.

[The author, in common with many others, neglects the possibility that the differences in incidence may have been due to differences in the concentration rather than the composition of the dusts in the collieries. The assimilation of the toxicity of silica and anthracite is contrary to all pathological evidence, and the differentiation of anthracite, steam, and bituminous coals is contrary to the finding by Heppleston (*Arch. industr. Hyg. occup. Med.*, 1951, **4**, 270) that the tissue reactions to these three dusts in the lungs of coal-miners are indistinguishable. It is difficult, however, to take this paper seriously, since the experimental results are presented in such a way that it is impossible to judge of their validity, and in any case frequently appear to contradict the author's own thesis, which is itself so vaguely expressed as to be almost meaningless.] *B. M. Wright*

1346. **Studies on Cotton Dust in Relation to Byssinosis. Part I. Bacteria and Fungi in Cotton Dust**
G. FURNESS and H. B. MAITLAND. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 138–145, April, 1952. 22 refs.

The inhalation of cotton dust leads to an asthmatic condition known as byssinosis which is characteristically worst on Monday mornings. This paper is the first of a series of studies of the composition of cotton dust in relation to byssinosis.

The material studied was air-borne dust collected by the air-cleaning plant in a factory and passed through a 90-mesh sieve. A detailed description of the bacteriological technique and findings is given [and should be read in the original by those interested]. A very large variety of organisms was found, nearly all of which were non-pathogenic, the exceptions being clostridia. No attempt was made to relate any particular one to the disease. *B. M. Wright*

1347. **Cardiovascular Disease in Cotton Workers. Part III. A Clinical Study with Special Reference to Hypertension**
R. S. F. SCHILLING, N. GOODMAN, and J. G. O'SULLIVAN. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 146–153, April, 1952. 1 fig., 25 refs.

In a previous paper (*Brit. J. industr. Med.*, 1951, **8**, 77) the authors showed that cotton workers exposed to the inhalation of fine cotton dust experienced a higher mortality from both cardiovascular–renal and respiratory disease than those not so exposed. The present study is concerned with the incidence of cardiovascular–renal disease and, in particular, of hypertension in groups of cotton workers with and without dust exposure. Mills were chosen in which it was considered that dust concentrations were high, and in these all men between 35 and 65 who had worked for at least 10 years in card- and blow-rooms and who had not been exposed to other dusts for any substantial period formed the experimental group, 103 in number. The control group consisted of 93 weavers and warehousemen working in the same towns and, where possible, in the same mills, but not exposed to cotton dust. The two groups were comparable in age and length of employment. A clinical history was

obtained from each man, and a clinical examination was carried out which included urine analysis, examination of heart and lungs, and blood-pressure recordings, which were repeated until a stable figure was obtained.

The incidence of rheumatic heart disease and renal disease was equally low in the two groups. The mean systolic and diastolic pressures in the two groups were similar at all ages except between 50 and 60, where both were higher in the group with dust exposure. At this age there was also a higher incidence of hypertension (systolic pressure 150 mm. Hg or more and diastolc pressure 90 mm. Hg or more) in the experimental group. Neither of these differences reached a statistically significant level, however, so more men of this age group from other mills, comparable with the original subjects, were examined. There were then 59 men in the experimental and 50 in the control group aged between 50 and 60, and statistically significant differences appeared in respect of the proportion with hypertension (25% in the experimental group and 8% in the control group) and in the mean systolic pressure level (137·9 mm. Hg in the experimental group, 129·9 mm. Hg in the control group). A similar but not significant difference appeared in the mean diastolic pressures.

The possibility is examined, and ruled out, that these differences were due to observer error, anthropometric differences, heredity, or renal disease undetected in the examinations. There was suggestive evidence of a relationship between the incidence of hypertension and the degree of industrial pulmonary disease among the experimental group, which is to be investigated more fully. *P. D. Oldham*

1348. **The Mechanism of Dispersion of Coal Particles in the Lungs of Miners**

A. POLICARD. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 108–111, April, 1952. 5 refs.

Conclusions drawn from studies of the disposition of dust particles in the lungs of animals cannot be satisfactorily applied to man owing to differences in the behaviour of their lungs, while similar studies in man are made difficult by the collapse of the lungs which occurs when the chest is opened post mortem. The case of a miner who was killed by fire damp while working in a coal mine provided an unique opportunity for such a study because the resultant pulmonary oedema prevented collapse of the lungs, the findings in which are reported.

Very few free dust particles were found in the alveoli, but there were many dust cells, filled to a varying extent with particles. Accumulations of dust cells were found in the periarterial and peribronchial tissues, and there was also some focal emphysema. The mode of transfer of the dust cells from the alveoli to these sites is discussed in detail and it is concluded that two processes are involved: " Some dust cells enter the pulmonary connective tissue at the level of the terminal bronchioles and reach the lymphatic channels normally present in the [periarterial and peribronchial] sheaths. So long as the sheaths are not abnormal, the dust cells are carried by the lymph and pass to the tracheo-bronchial glands. Other dust cells formed in the alveoli adjacent to the sheaths penetrate them from outside. They are found in the periphery of the sheaths. It seems that the dust cells remain stationary and are not carried to the lymph nodes. The anthracotic nodule appears to result from the growth of sheaths thickened in the following way. At the periphery of the sheaths the alveoli collapse. Their walls are applied to the external surface of the sheaths which is thickened by them. The dust cells which happen to be in the alveolar cavities are thus included in the thickened wall of the sheaths, that is to say, in the outer part of the anthracotic nodule. The dust cells thus included in the nodule seem destined to remain permanently fixed there."

The author emphasizes that these conclusions are only indirect deductions from morphological observations.

B. M. Wright

1349. **A Sampling Procedure for Measuring Industrial Dust Exposure**

P. D. OLDHAM and S. A. ROACH. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 112–119, April, 1952. 11 refs.

In order to relate medical findings to dusty conditions of work it is necessary to evolve a method of estimating the dose of dust inhaled over a number of years. The main difficulties arise in: (*a*) the variability of dustiness in the place of work; and (*b*) the turning of measured concentrations into measure of dosage which may be compared with indices of disease. The data needed are: the men actually at risk; the mean concentration of respirable dust where they work; and the duration of their exposure. For precise estimation it is necessary that a full programme of sampling be planned at each man's working-place. The use of average figures for a larger area of the environment may introduce a high error.

Coal-mining does not proceed with the uniform regularity of other occupations, and during intervals (for example, for technical breakdowns) the dust concentration may rapidly become insignificant. Further variables, such as the time taken to reach the coal face and the effect of absenteeism, are mentioned and the errors which may result are discussed. To overcome this difficulty the " random colliers " sampling method has been evolved. Men chosen at random from the group to be studied are followed with the sampling instrument, and dust-samples taken at random times. If possible each man in the group should be followed for one full shift. The variability of concentrations is offset by the fact that the probability that a particular concentration will be sampled is proportional to the time it endures. The difficulty of deciding when to start or end sampling is met by this method, for it is concerned with only one man at a time. Absenteeism is allowed for, for if the chosen man is absent no samples are taken; redistribution of the men to meet absenteeism is taken into account, in that the man chosen for a shift may be among a number so redistributed.

A practical example of the use of the method is given, with a table of results. A mean dust concentration and a mean duration of exposure (that is, the grand mean

of all observed lengths of shift, less break-times) are obtained; the product of these gives the figure for particle-hours per ml. It is assumed that the volume of air breathed per minute is constant. The application of the method to long-term surveys is also described.

L. W. Hale

1350. **Dust Sampling and Lung Disease**

C. N. DAVIES. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 120–126, April, 1952. 4 figs., 12 refs.

Selective dust sampling, by collecting only the finer and more dangerous particles, may be expected to yield samples in which the mass of particles may serve as an index of the risk. If the sampling instrument can select the range of size automatically, much microscopical work is avoided, and the results can be analysed by simple weighing. The method is limited to dusts whose chemical action is slow, and whose liability to evaporation or chemical change in the air is low. The ideal sample would be free of all particles which would have been deposited elsewhere than in the alveoli, and though the need for further study of size distribution would not of course be entirely removed, there would probably be a correlation between disease incidence and mass in such a dust sample.

The process of dust retention in the alveoli is discussed. It is suggested that particles are deposited in the larger bronchial tubes by impingement, with a gradual transition to sedimentation in the small bronchioles and alveoli. Particles 0·2 to 1·5 μ in diameter are retained almost entirely in the alveoli and respiratory bronchioles. By assuming that the exchange of fine particles between alveolar and tidal air is similar to that of gases it has been possible to plot curves for particles retained (*a*) in the alveoli, and (*b*) above the alveoli, by plotting percentage retention against particle diameter. The results by this method are compared with the figures of other workers and good agreement is found in respect of alveolar retention of particles below 1 μ in diameter. Above 1 μ coal particles seem to be retained more abundantly than quartz (possibly because they stimulate less phagocytosis).

The effect of variation in breathing is then considered. In normal respiration 15% of the alveolar air is expelled, but in maximal respiration this rises to 70%; this directly affects the proportion of particles that reaches an alveolus. The proportion that remains there is also affected by the frequency of respiration. In view of the tendency of these functions to cancel each other out, however, the rate of working does not rapidly affect degree of alveolar retention.

With this knowledge of the size-selecting properties of the lung in mind, the author makes suggestions for the design of a sampler which would collect " alveolar " dust, and could be used for assessing risks due to inhalation of particles which dissolve or react only slowly. [The toxicity factor is not considered.] Such a selector should be able to collect 50% of all particles 5 μ in diameter, increasing to 92% of particles 2 μ in diameter, size separation being performed by elutriation. Samples taken after treatment of dust by such a selector would approximate to alveolar sampling.

L. W. Hale

1351. **The Toxicity of Inhaled Aluminium Hydrate and its Action on the Pulmonary Tissues.** (La nocivité de l'hydrate d'alumine en inhalation et son action sur le tissu pulmonaire)

G. JULLIEN, E. VALLECALLE, and M. LEANDRI. *Archives des Maladies Professionnelles* [*Arch. Mal. prof.*] **13**, 31–38, 1952. 3 figs., 2 refs.

The authors review previous work on the effect of aluminium on the solubility of silica and on experimental silicosis. They consider also the various attempts to apply these findings in the field, the criticisms of them which have been made, and especially the claims of some German workers that aluminium is itself capable of producing pulmonary disease. They then report the results of an experimental study of the effect of inhalation of aluminium hydroxide powder on the lungs of guinea-pigs. The animals were " exposed to inhalations of aluminium hydroxide ranging from 5 to 90 hours for a week to 7 months " [the meaning of this statement is obscure in the original; no details of the method of exposure are given]. The animals' lungs showed the usual reaction to dust inhalation, namely, the presence of dust cells in the alveoli and the peribronchial and perivascular deposits. Various other reactions were observed of which the most important was a thickening and hyperplasia of the alveolar walls. The authors discuss their findings and conclude that although no fibrosis was produced, aluminium hydroxide is potentially toxic when inhaled.

B. M. Wright

1352. **A Follow-up in 1950 of 463 Cases of Silicosis admitted to the Industrial Medicine Clinic of the University of Milan between 1943 and 1947.** (Situazione nel 1950 di 463 silicotici ricoverati in clinica del lavoro dal 1943 al 1947)

G. BALDI. *Medicina del Lavoro* [*Med. d. Lavoro*] **43**, 147–159, April, 1952.

In a follow-up in 1950 of 539 cases of silicosis examined at the University Industrial Medicine Clinic in Milan between 1943 and 1947, 463 patients were traced, of whom 212 had died. The cause of death was known in 98 of the 212, 69 having died of silico-tuberculosis and 16 of heart failure secondary to silicosis. The 463 traced patients were classified on the basis of the initial radiograph into cases of reticular fibrosis (11%), nodular silicosis (44%), massive silicosis (33%), and silico-tuberculosis (12%). The results were analysed to show the effect upon prognosis of the initial radiological stage, occupation before the first attendance, and occupation during the period of follow-up. There was a steady deterioration in prognosis in proceeding from the patients with reticular fibrosis to those with silico-tuberculosis, of whom 89% had died. The worst prognosis in terms of fatality and radiological progression was found in miners and workers engaged in grinding quartz. The lowest mortality and progression was found in foundry labourers. Evolution was also more rapid in

those workers who contracted the disease after a short time of exposure to risk in especially dangerous occupations than in those in whom it appeared after more than 25 years' work. [There is no comment on the inevitable confusion between age and industrial exposure here.] Among the 251 survivors the effect of occupation during the period of follow-up was studied, and the results are given in the following table:—

Initial Form of Silicosis	Number of Cases		Stationary %		Progression %		Severe Progression %	
	A	B	A	B	A	B	A	B
Reticular	22	22	50	32	50	45	—	23
Nodular	44	105	34	23	59	53	7	24
Massive	12	40	17	15	58	55	25	30
Silico-tuberculosis	—	6	—	(17)	—	(83)	—	—

A = Continuing in dusty employment.
B = Not continuing in dusty employment.

The author concludes that " the evolution of nodular and massive silicosis appeared to be unconnected with cessation or prolongation of work in a dusty environment ". [In fact the figures given in the table suggest that progression was more severe in those who left their previous work. Presumably these patients were more severely ill, so that the two groups are not comparable.] He also concludes that in giving advice concerning the desirability of any patient's continuing to work in a dusty atmosphere the rapidity of the onset of silicosis must be considered. Those in whom the disease sets in in a relatively rapid form should be withdrawn, particularly in the early stages. The danger of a given occupation must be judged not only in terms of the prevalence of silicosis, but also of the usual rapidity of evolution of the disease. Prognosis, as well as present disability, should be considered in assessing compensation in cases of silicosis. *C. M. Fletcher*

1353. **Pneumoconiosis of Coal Miners in North East England with Special Reference to the Durham Coalfield** R. I. McCallum. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **9**, 99–107, April, 1952. 2 figs., 22 refs.

The author reviews the history of pneumoconiosis among coal-miners in north-east England, concluding that a severe form of the disease must have arisen while the industry was expanding during the 19th century, but that improvements in ventilation subsequently reduced the incidence and severity of the disease. During the past 10 years there has been an increase in the number of cases diagnosed by the Silicosis Medical Board: this may be due to improvements in diagnosis and increased awareness of the disease rather than to increase in prevalence or severity. A review is then given of the findings of a mass miniature radiography survey of pits in the Durham coalfield. The author points out the disadvantages of this method for establishing the prevalence of pneumoconiosis, those examined being volunteers representing only 40 to 60% of the working population of the mines, and serious errors in the diagnosis of early pneumoconiosis arising from the use of miniature films. In a comparison of readings by the same observer of miniature and large films of 102 patients, only in 40% was there agreement between the two. A considerable number of men with radiological signs of pneumoconiosis may therefore be missed in a survey with miniature films and not referred for a large-film examination. Large-film radiographs of 1,468 men from 8 mines in County Durham who had been so referred out of a total of 7,937 were classified according to the system used by the Pneumoconiosis Research Unit of the Medical Research Council. It was found that the number with pneumoconiosis of Category 2 or more represented between 3·3% and 8·5% of the men attending for miniature radiography.

There was very little complicated pneumoconiosis. The prevalence of pneumoconiosis increased with age up to 40 and thereafter remained relatively constant.

It is concluded that there is fairly widespread prevalence of pneumoconiosis in this coalfield, but that its severity is much less than in the South Wales coalfield. Further surveys, using large films instead of miniature films, are necessary to confirm the findings recorded in this paper, and would help to ensure that the progressive mechanization of coal-mining in this coalfield is not increasing the prevalence of pneumoconiosis by raising dust concentrations. Such surveys might also establish whether dust suppression methods are effective. *C. M. Fletcher*

1354. **Pneumoconiosis in Boiler Scalers**
L. Dunner, M. S. Hicks, and D. J. T. Bagnall. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **46**, 43–49, Jan., 1952. 8 figs., 8 refs.

Pneumoconiosis is not uncommon in men engaged in scaling the boilers of ships, and the authors describe 25 cases seen at Hull. The working conditions in this job are far from good: the space is confined and the air is full of dust. This dust is of two kinds: (*a*) boiler scale dust; and (*b*) flue dust (soot). Analysis of the former indicated a free silica content of 1·1% and of the latter up to 10·5%; iron dust was also present.

Individual susceptibility to the development of pneumoconiosis varied; symptoms also varied and were not always proportional to the radiological appearances. Melanoptysis (black sputum) was sometimes observed; this was ascribed to cavitation of black foci in the lung. The radiological appearances varied from " increased linear striation " to nodulation (stated to be not always bilateral or symmetrical); in some cases there was nodulation with typical coalescent masses. A pattern of irregular running strands of fibrosis is also described. The chief complications were tuberculosis (4 cases) and carcinoma (4 cases, 3 of primary bronchial carcinoma).

The relation between the radiological findings and the morbid anatomy is discussed, but as the data were incomplete no clear correlation was possible; in one case typical silicotic nodules were seen at necropsy. It is pointed out that in Great Britain boiler scalers are not at present eligible for compensation. *L. W. Hale*

Forensic Medicine and Toxicology

1355. **Chronic Mercury Poisoning in Latent Finger-print Development**
G. Forbes and J. White. *British Medical Journal* [*Brit. med. J.*] **1**, 899–902, April 26, 1952. 1 fig., 4 refs.

Policemen engaged in securing and photographing finger-prints use "grey powder" (hydrargyrum cum creta, *B.P.*) as a dusting agent. This has been shown on two recent occasions, in Lancashire and in Sheffield, to involve the risk of mercury poisoning. It is believed that the method of absorption is by inhalation of mercury vapour, or by ingestion of minute particles, or through the skin. Of 5 Sheffield policemen employed almost entirely in the finger-print department, 2 suffered from mercury poisoning, with tremors, sweating, and muscular weakness. There appeared to be a big difference in personal susceptibility; but apart from idiosyncrasy, some workers used the powder sparingly and cautiously and others more lavishly. Also personal care and cleanliness varied among these workers as among most other workers. *G. F. Walker*

1356. **The Relation of the Alcohol Content of the Blood to that of the Expired Air.** (Zur Frage der Relation von Blutalkohol zum Atemalkohol)
P. Seifert. *Archiv für Experimentelle Pathologie und Pharmakologie* [*Arch. exp. Path. Pharmak.*] **214**, 427–432, 1952. 7 figs., 3 refs.

The relation between the blood alcohol content and the concentration of alcohol in the expired air has been studied at the Institute of Forensic Medicine of the University of Heidelberg. The alcohol content of the breath was estimated by the method described by Seifert and Gunther (*Arch. exp. Path. Pharmak.*, 1951, **213**, 37) in which, by means of a spirometer-type mouthpiece, expired air is passed through a gas-meter into a solution of potassium permanganate in dilute sulphuric acid. If there is no alcohol in the air, the solution does not begin to change colour until about 20 litres of expired air has passed through it, whereas a much smaller volume of air containing alcohol vapour will decolorize the permanganate, the volume required depending on the concentration of alcohol present. In 17 experiments on 6 subjects the alcohol concentration in the blood and breath was estimated at 3- or 5-minute intervals after the subject had drunk a dose of 0·8 g. of 30% alcohol per kg. body weight at various intervals after taking food.

In all cases the changes in blood alcohol concentration were faithfully reflected in the breath, and from the results of these and previous experiments an average curve was plotted relating the blood alcohol concentration to the volume of expired air required to cause a detectable change in colour of the permanganate solution, concentrations ranging from 0·1 to 1·5 mg. of alcohol per ml. of blood corresponding roughly to decolorizing volumes ranging from 2·0 to 0·45 litres. This relationship is almost linear for blood concentrations between 0·5 and 1·2 mg. per ml., each change of 0·1 mg. per ml. being associated with a change of about 70 ml. in the required air volume. When the blood alcohol concentration is more than 1·2 mg. per ml., however, the experimental error, which remains constant at about 40 to 50 ml. of air, seriously reduces the accuracy of the permanganate method, while at lower concentrations the end-point becomes less easy to define as the colour change occurs so slowly.

It is claimed that the sensitivity and simplicity of the method makes it suitable for use in assessing the degree of alcoholic intoxication in an objective manner.
Derek R. Wood

1357. **Nitrite and Thiosulfate Therapy in Cyanide Poisoning**
K. K. Chen and C. I. Rose. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **149**, 113–119, May 10, 1952. 1 fig., 52 refs.

A comparison is given of the effects of antidotes in cyanide poisoning in dogs, the LD50 of sodium cyanide in untreated dogs being taken as the figure 1. Treatment with sodium thiosulphate alone tripled the LD50, amyl nitrite alone raised it to five times the level, sodium nitrite alone had the same effect, amyl nitrite plus sodium thiosulphate multiplied it by 11, while sodium nitrite immediately followed by sodium thiosulphate raised it 18-fold. Detoxification depends upon: (1) the formation of methaemoglobin by nitrite action; (2) the successful competition for cyanide ions by methaemoglobin with the respiratory enzyme ferricytochrome oxidase; and (3) the conversion of cyanide to thiocyanate by the action of the enzyme rhodanase.

The authors report 16 cases of cyanide poisoning, 4 of which were treated successfully with nitrite alone and 12 with nitrite and thiosulphate; to these they add another 28 cases collected from the literature, giving a total of 44 cases with only one death. It is recommended that the drugs be given intravenously in doses of 10 ml. of a 3% solution of sodium nitrite (0·3 g.), immediately followed by 50 ml. of a 25% solution of sodium thiosulphate (12·5 g.). Both of these drugs decompose in water, but remain stable for years if an anti-oxidant such as sodium sulphite is added. The drugs also keep well in ampoules in a dry place, and they can be dissolved in water when needed. It is emphasized that the materials for nitrite–thiosulphate therapy should be at hand as treatment must be given speedily: inhalations of amyl nitrite should be given by the first competent person to arrive on the scene. Artificial respiration must be started at once if breathing fails. *M. A. Dobbin Crawford*

Anaesthetics

1358. **Succinylcholine Chloride: an Ultra-short-acting Relaxant**

A. P. Balthasar and C. A. Sara. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 540–542, April 19, 1952. 8 refs.

The authors describe their experience with succinylcholine chloride in a series of patients [number unspecified] whose ages ranged from 6 years to 67 years. Their observations confirm those of earlier workers, namely, that the action of the drug is short and that succinylcholine is therefore a suitable relaxant for orthopaedic manipulations, electric convulsion therapy, and intubation; it does not cause side-effects on the cardiovascular system, and there is relative freedom from histamine liberation.

The unpleasant subjective effects of succinylcholine are emphasized, and in an attempt to overcome these the authors ascertained the proportion of the drug which would stay in solution with thiopentone and the length of time the resultant mixture would retain its relaxant potency; this was found to be 30 minutes with thiopentone in excess in the ratio of 2:1. They state that in electric convulsion therapy the paralysing effect had completely disappeared after 5 minutes. Less thiopentone was needed with succinylcholine than with the other drugs to produce the relaxation necessary for intubation.

Donald V. Bateman

1359. **Succinylcholine (Succinoylcholine). Muscle-relaxant of Short Action**

J. G. Bourne, H. O. J. Collier, and G. F. Somers. *Lancet* [*Lancet*] **1**, 1225–1229, June 21, 1952. 2 figs., 27 refs.

In view of the need for a very short-acting relaxant for the purposes of intubation, electric convulsion therapy, and orthopaedic manipulation, the authors gave succinylcholine a trial in 546 cases in patients whose ages ranged from 3 to 86 years. The chemical properties of the drug and its mode of action and relation to other relaxants are described. Succinylcholine is found to resemble decamethonium in its mode of action rather than D-tubocurarine. However, it differs from decamethonium in being destroyed by cholinesterases, so that neostigmine (which inhibits cholinesterases and which is so useful in stopping short the action of D-tubocurarine and of gallamine) is contraindicated as an antidote. The side-effects of succinylcholine in normal doses are insignificant, though in very large doses it tends to raise the blood pressure. Its histamine-liberating activity, as investigated by intradermal injection in man, is very slight, being only one-hundredth of that of D-tubocurarine. It is also free from toxicity.

The technique used by the authors is as follows. Light premedication is given, except in the case of children; anaesthesia is induced with thiopentone and maintained with nitrous oxide and oxygen, supplemented with thiopentone where necessary. A 5% solution of succinylcholine is given intravenously, the usual dose being 1·0 ml. per 100 lb. (0·022 ml. per kg.) body weight. The injection first produces a diffuse uncoordinated contraction of muscle bundles and groups of muscles coming on 12 to 15 seconds after the injection or earlier in children, and the onset of paralysis is indicated by the cessation of these movements. Paralysis normally lasts 2 to 6 minutes and muscle power has fully returned in a further 3 to 4 minutes. Respiratory arrest always occurs with effective doses, and this is counteracted by rhythmical inflation of the lungs with oxygen, or with nitrous oxide and oxygen for longer operations. In only 5 cases was the apnoea prolonged for more than 5 minutes, and in none for more than 15 minutes.

The use of succinylcholine was remarkably free from side-effects in normal effective doses. Salivation was copious only in patients subjected to instrumentation of the mouth and pharynx and to whom no atropine or scopolamine was given. More or less detailed descriptions of the technique adopted for a number of short procedures are given, and a few cases of greater magnitude involving abdominal relaxation are described.

Edgar J. Gatt

1360. **Self-experiments with Succinylcholine Chloride. A New Ultra-short-acting Muscle Relaxant**

O. K. Mayrhofer. *British Medical Journal* [*Brit. med. J.*] **1**, 1332–1334, June 21, 1952. 20 refs.

The author reports the results of six experiments, carried out on himself, with a new muscle relaxant, succinylcholine chloride. The drug was given intravenously, and artificial respiration was administered by an anaesthetic machine. In the first experiment 0·125 mg. of succinylcholine chloride per kg. body weight was injected within 2 seconds; 30 seconds later muscular weakness set in, followed at one minute by partial respiratory paralysis and difficulty in speaking; 2 minutes after the injection the effects were beginning to wear off and were gone completely one minute later. No artificial respiration was necessary and the blood pressure and pulse showed no change. In the second experiment double the initial dose, also injected within 2 seconds, produced similar but more marked effects. Artificial respiration had to be maintained for 50 seconds; no objective or subjective effect was apparent 4 minutes after the injection. Three times the initial dose in the third experiment caused painful fibrillary muscle twitching and complete skeletal paralysis in under one minute. Respiration was assisted for 70 seconds, and the effect had worn off in 4 minutes. The electrocardiogram showed practically no change in the heart action. In

the fourth experiment 0·25 mg. per kg. body weight was injected slowly within 2 minutes; 90 seconds from the start of the injection double vision developed, speaking was difficult, and the extremities could be moved with a little difficulty; the effect had worn off after 150 seconds. In the fifth experiment a dose of 0·5 mg., also given slowly over 2 minutes, produced more intense effects and respiration had to be assisted for 50 seconds; no objective or subjective effect was observed after 4 minutes.

In the last experiment a continuous infusion of a 0·2% solution in normal saline was given for 5 minutes at a rate equivalent to a dose of 0·06 mg. per kg. per minute. The onset of muscular weakness was noted 2 minutes from the start of the infusion, which was followed one minute later by marked ptosis and almost complete intercostal paralysis; no assisted respiration was necessary; 2 minutes after the infusion had been stopped the effect had almost completely worn off. About 10 minutes later the infusion was started again, but the dose was doubled. Total paralysis resulted in 2 minutes, but the blood pressure and electrocardiogram showed no significant changes.

On the basis of these experiments the author recommends the drug for use in abdominal and thoracic surgery, to facilitate endotracheal intubation to overcome severe laryngeal spasm, and as an adjuvant in electric convulsion therapy. *Norval Taylor*

1361. **The Ultra-short-acting Relaxants**
H. RICHARDS and H. R. YOUNGMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1334–1335, June 21, 1952. 10 refs.

The authors present a report on the use of succinylcholine in 250 cases. In adults, who were usually given 100 mg. of succinylcholine iodide, paralysis was maximal within one minute, the onset being preceded by general fibrillary twitching for a few seconds. No other side-effect was observed and recovery was rapid, the time from the first sign of spontaneous respiration to recovery of all reflexes being not more than 3 minutes.

Complete paralysis of the vocal cords, lasting long enough for an unhurried intubation, resulted when 100 mg. of succinylcholine iodide was given after 0·5 g. of thiopentone had been administered. The combination of full relaxation, light anaesthesia, and rapid recovery was found to be useful during manipulation and reduction of fractures. The authors draw attention, however, to the danger of profound relaxation and a full stomach. Succinylcholine was as satisfactory during cephalic version as gallamine triethiodide; recovery was more rapid and no antidote was necessary. In electroplexy the shock was given one minute after administration of the relaxant, the lungs being inflated with oxygen during the short period of apnoea. Succinylcholine did not interfere with the effect of other relaxants used subsequently.

Full relaxation was maintained with a continuous infusion of a 0·1% solution given at a rate equivalent to about 4 mg. a minute, light anaesthesia being continued by any method suitable for the particular case.
Norval Taylor

1362. **Anesthesia and the Cardiac Patient**
G. W. HAYWARD. *Anaesthesia* [*Anaesthesia*] **7**, 67–71, April, 1952. 7 refs.

The author assesses the operative risks of major surgery in patients with heart disease as being only a little higher than in those without heart disease provided full advantage is taken of up-to-date surgical and anaesthetic techniques. He regards two factors as of especial importance—anoxia and hypotension. " Myocardial anoxia if long continued will cause signs of myocardial insufficiency in patients who previously showed no signs of heart failure." He considers that sudden death is most likely to occur in patients with coronary disease, aortic stenosis, syphilitic aortitis, heart-block, or a large patent ductus arteriosus; " death is usually the result of ventricular fibrillation in these patients ". Preoperative treatment with procaine amide hydrochloride (" pronestyl ") is advised in a dosage of 500 to 1,000 mg. orally; if cardiac irregularity occurs during operation the drug may be given intravenously at a rate not exceeding 100 mg. per minute up to a total dose of 1,000 mg.

It is pointed out that controlled hypotension is regarded by cardiologists as particularly dangerous in elderly arteriosclerotic patients or in those with coronary disease, but that too little is known about the effects of this technique for a balanced opinion to be given. " Provided the coronary arterial system is healthy, it is unlikely that coronary insufficiency will appear if hypotension is produced by ganglionic blocking drugs, as in spite of a decreased coronary blood flow, the work of the heart and the metabolic needs of the cardiac muscle are reduced in proportion ", this being in direct contrast to the hypotension of haemorrhage. It is stated that whereas hypotension can be avoided in those with a history of angina pectoris or other suggestive signs of coronary impairment, it is not uncommon for coronary insufficiency to be silent until myocardial ischaemia occurs during operation, and there is no reliable way of detecting it preoperatively. In view of such unpredictable risks it would therefore seem wise at present to restrict the use of controlled hypotension to operations where success depends on a bloodless operative field, thus justifying acceptance of the increased risks involved.

It is recommended that in congestive heart failure operation be postponed until the heart rate has been stabilized, but when urgency precludes this, immediate administration of " digoxin ", 1 mg. intravenously or 1·5 to 2 mg. orally, is advised; pulmonary congestion should be counteracted by careful control over the fluid balance and the use of mercurial diuretics. As the author says, " one method of treating or preventing attacks of acute pulmonary oedema in man is the administration of a rapidly acting barbiturate ".

Cardiac arrhythmias are not considered to call for specific measures beyond normal care; and it is suggested that angiocardiography is best performed under basal narcosis in adults, but under general anaesthesia in children.

[The author is to be congratulated on a very concise review of the subject which is a valuable and practical contribution.] *Michael Kerr*

Radiology

RADIOTHERAPY

1363. **Clinical Experience with Irradiation Through a Grid**
H. MARKS. *Radiology* [*Radiology*] **58**, 338–342, March, 1952. 19 refs.

The author gives a short review of grid irradiation methods, beginning with the work of Kohler in 1909. For the use of grids to be successful he considers that lead-rubber should be used to prevent secondary radiation damaging the covered skin, and that the open areas should amount to 40% of the whole, with the apertures of the grid overlying the same areas of skin at each exposure. Daily doses of 400 to 800 r, measured in air, are used by him to a total of 10,000 r with a grid of 20×20 cm., or 12,000 r with a grid of 10×15 cm. With these levels of dosage a confluent desquamation results, the grid pattern having disappeared by the end of the treatment. The reaction lasts 4 to 10 weeks. The author emphasizes that the general well-being of the patient during treatment is of first importance, and that such patients should be seen personally by the radiologist to check their condition daily. He has treated 200 patients by the grid method, of whom 102 completed their treatment. These included cases of many types of tumour, all said to have been large. Of the patients treated, 25 remained symptom-free up to the time of the report, some for 3 or 4 years or more.

(The technical factors used were: H.V.L., 0·9 mm. Cu; F.S.D. 50 cm.; 10 mA; 27·5 r per minute.)

J. M. Gibson

1364. **Recent Clinical Experience with the Grid in the *X*-ray Treatment of Advanced Cancer. Preliminary Report**
W. HARRIS. *Radiology* [*Radiology*] **58**, 343–350, March, 1952. 2 figs., 9 refs.

This is a preliminary report on the treatment of 149 patients with large, incurable tumours by the grid technique in the Radiotherapy Department of the Mount Sinai Hospital, New York. A 40% open grid of 4-mm. lead-rubber was used, with round apertures 0·5, 1·0, and 1·5 cm. in diameter. The use of the smallest of these grids was given up as impracticable, and on irregular surfaces the 1·5-cm. grid was always used; 3% of the incident radiation was transmitted to the protected skin. The technical factors used in almost all these cases were: 200 kV; H.V.L., 0·9 mm. Cu; F.S.D., 50 cm. Two or even 3 fields were used. Bone and cartilage appeared to withstand high doses, but the author states that damage to the intestine may be expected if it receives more than 6,000 r. He does not cite any cases in which such damage did occur, though mentioning 4 patients who received high doses to the abdomen without ill effects. Pulmonary fibrosis, on the other hand, developed frequently and often very rapidly, even within 2 months.

The author considers that by using the grid technique it is possible to deliver a higher dose to the tumour than is possible by conventional methods without a severe reaction. He considers that for palliative therapy this method is useful, particularly in cases of carcinoma of the lung or urinary bladder. *J. M. Gibson*

1365. **The Results of Radium and *X*-ray Therapy in 124 Cases of Epithelioma of the Residual Cervix Treated at the Curie Foundation from 1919 to 1944.** (Les résultats de la radiothérapie (curiethérapie et roentgenthérapie) de 124 cas d'épithéliomas sur col restant traités dans les services de la Fondation Curie, de 1919 à 1944 inclus)
J. BAUD. *Bulletin de l'Association Française pour l'Étude du Cancer* [*Bull. Ass. franç. Cancer*] **43**, 100–104, 1952.

During the 26-year period from 1919–44, 2,688 cases of epithelioma of the uterine cervix were treated at the Curie Foundation in Paris, of which 124 cases (4·6%) were of epithelioma arising in the cervical stump after subtotal hysterectomy for some non-malignant condition.

The distribution of cases according to the international classification was as follows: Stage I, 25 cases (20%); Stage II, 59 cases (47%); Stage III, 33 cases (27%); Stage IV, 7 cases (6%).

The treatment was identical to that used for cervical epitheliomata of the intact uterus, that is: (1) radium application and pelvic irradiation by *x* rays or by teleradium (98 cases); (2) radium application alone (15 cases); and (3) pelvic irradiation only (11 cases).

The results are given as follows: 51 patients remained symptomless 6 to 22 years after treatment; 3 patients are still alive, but not cured, after more than 5 years (6, 7, and 9 years respectively); 52 patients died of the epithelioma within 6 to 24 months; 15 patients developed local and pelvic recurrences, the survival period varying from 3 to 4½ years; 2 patients have been lost sight of 3 years after treatment; and one patient died from intercurrent carcinoma of the stomach.

The results are also analysed according to the technique of treatment: (1) Radium application only: 15 patients, in 9 of whom (3 Stage I, 2 Stage II, 4 Stage III) it was impossible to introduce a cervical applicator and intravaginal application only was possible; 5 cures (patients symptom-free after 6 to 17 years) were obtained. Of 6 other cases (all Stage I), in which a short radium applicator was introduced into the cervix, in 3 the patient was free from disease after 9 to 16 years. (2) Radium plus *x* rays: 50 cases. In 43 cases the radium was applied intravaginally, and 20 of these patients were symptomless after 6 to 20 years. In 7 cases radium was also applied to the cervix; 3 patients remained cured after 5 to 10 years. (3) Local radium therapy plus teleradium: 48 patients, of whom 20 were free from disease 6 to 22 years later. (4) *X* rays alone: 6 cases; no

cures were obtained. (5) Teleradium alone: 5 cases; no cures.

The author concludes with the following observations: (1) Epitheliomata of the cervical stump do not differ in any respect from those arising in a non-operated uterus. (2) The technique of radiotherapy is identical in both. The impossibility of introducing intracervical applicators does not diminish the chance of cure. (3) The proportion of cures is similar to that obtained in epitheliomata of the cervix of the intact uterus. *L. G. Capra*

1366. **Radiocobalt in the Treatment of Bladder Tumors**
J. W. SCHULTE, F. HINMAN, and B. V. A. LOW-BEER. *Journal of Urology* [*J. Urol.*] **67**, 916–924, June, 1952. 8 figs., 4 refs.

At the University of California a technique for the treatment of bladder tumours with radioactive cobalt has been evolved. The results of treatment of such tumours are disappointing, hence the continual trial of new techniques is justified. The rationale of this method is based on the dose distribution from a centrally-located point source of radiation. Radiocobalt is available in any desirable strength and its beta radiation, being of low energy, is easily screened, while its gamma radiation is almost entirely monochromatic.

To eliminate cystostomy or use of a three-way catheter a special catheter has been constructed to hold the cobalt "bead" and permit outflow of urine. A balloon surrounds the catheter and this is filled with 50 ml. of a weak solution of sodium iodide to which a few drops of methylene blue are added. Radiographs are taken in order to ascertain symmetry of the bag and to measure the distance from bead to tumour. In a 100-hour exposure 6,000 r is delivered at a distance of 2 to 2·5 cm. from the bead. If examination reveals residual tumour at the end of 6 weeks, the dose may be repeated. Reactions are less severe than with *x*-irradiation, and consist of erythema and symptoms of burning and frequency. These are more severe if a second application is necessary.

Papillomata and other localized tumours respond more often than infiltrative tumours. Research continues on the treatment of multiple papillomata and advanced infiltrative lesions. Of 13 patients followed up long enough for evaluation of immediate results, 6 received some benefit, but only 1 has remained free of recurrence. *I. G. Williams*

1367. **The Therapeutic Use of Radioactive Cobalt in the Form of Beads.** (Strahlentherapeutische Anwendung von radioaktivem Kobalt in Form von Perlen)
J. BECKER and K. E. SCHEER. *Strahlentherapie* [*Strahlentherapie*] **86**, 540–547, 1952. 13 figs., 4 refs.

From the Czerny Hospital for Radiotherapy, Heidelberg, a method of intracavitary irradiation employing threaded beads of radioactive cobalt is described. The beads have a diameter of 4 to 7 mm., and are available in activities of 2·5 mc., 5 mc., and 7 mc. Three main advantages are claimed for this method: (1) the beads can be introduced through even the smallest aperture; (2) they assume the shape of the cavity to be irradiated; (3) they fill homogeneously the entire volume of the cavity.

The method has been employed chiefly for the treatment of carcinoma of the corpus uteri. The beads, threaded on nylon string, are introduced into the uterine cavity through a tube inserted into the cervical canal. [The method is, in fact, a minor variation of Heyman's "packing method".] A similar method is used when treating vesical cancer in females. The string of beads in these cases may usefully contain a number of non-active spacing beads to give a homogeneous radiation distribution throughout the bladder cavity. An attempt is being made at present in cases of localized bladder lesions to guide the intravesical cobalt beads to the affected site and keep them there by means of a strong electromagnet applied to the body externally.

For intracavitary irradiation of oesophageal tumours the following method is employed. The patient is made to swallow a lead bead to which a silk thread is attached. The bead reaches the large intestine within 3 days. At this stage a metal ring approximately 4 mm. in diameter is attached to the silk thread, and a double nylon thread is passed through the ring, which is gradually drawn into the stomach. One free end of the nylon thread is now tied to a string of the radioactive cobalt beads, and these are drawn into the correct position in the oesophagus under fluoroscopic control by pulling on the other free end of the nylon thread. The correct position of the beads in the oesophagus is maintained by strapping the double nylon thread to the cheek. For surface irradiation of benign and malignant cutaneous lesions the beads are embedded into pliable plastic material. In this way it is said to be possible to treat surface lesions of irregular outline, even if situated on a curved surface, with ease and accuracy. *Jan G. de Winter*

RADIODIAGNOSIS

1368. **Rontgenologic Aspects of Meningiomas**
E. P. PENDERGRASS and C. R. PERRYMAN. *British Journal of Radiology* [*Brit. J. Radiol.*] **25**, 225–234, May, 1952. 10 figs., 15 refs.

The authors found that of 1,300 cerebral tumours verified at the Hospital of the University of Pennsylvania, 15% were meningiomata. These could be classified into two gross pathological types, the massive or global type which invaginates the pial membrane into the brain and may become buried, and the type *en plaque* which grows along the plane of the meninges. Both types tend to invade the bones of the skull, and both vary in vascular pattern and texture.

The radiological appearances are those of destruction of and hyperostotic changes in the cranial bones overlying them. The latter may be diffuse or nodal, and may be accompanied by swelling of the cranium and displacement of organs such as the eyeballs. The tumour may extend through the bone and invade the soft tissues; it may be retarded, but is not limited, by the sutures. The appearance of increased vascularity of the bone, which may be the only sign, is of significance only if it is unilateral and compatible with clinical signs and symptoms. More extensive changes are produced by tumours

en plaque and these have to be differentiated from eburnated osteomata; the latter, however, do not as a rule cross suture lines.

The classifications of bone changes made by Rowbotham in 1939 is discussed and correlated with the authors' own observations. They suggest that meningiomata lend themselves well to classification according to their location, and divide them into those involving the sphenoidal ridge, the suprasellar region, the olfactory groove, the base of the skull, and the parasagittal areas. The radiological signs and the clinical symptoms and signs are described, and the differential diagnosis is discussed. Mention is made of 3 cases in which a meningioma adjacent to the Gasserian ganglion was discovered during operation for trigeminal neuralgia. Meningiomata without dural attachment may, it is suggested, originate in the arachnoid; these may be divided into: (1) intraventricular tumours arising from the choroid plexus; (2) subcortical tumours arising from the lateral margin of the tela choroides; (3) tumours arising deep in the Sylvian fissure; and (4) subtentorial tumours of inconclusive origin.

Finally, meningiomata of the cerebellar chamber, which are found more often in women, are discussed. The radiological findings are those of increased pressure, hyperostosis, pressure erosion, and calcification. Those in the region of the acoustic foramen may produce erosion of the petrous bone and are difficult to differentiate from acoustic neuromata. Multiple meningiomata may occur in this region; these multiple meningiomata occur more frequently than is generally realized. One tumour usually predominates, and careful study of the radiographs may reveal it as the only clue to the presence of others. *W. B. D. Maile*

1369. **Radiodiagnosis of Eosinophilic Granuloma.** (Contributo allo studio radiologico del granuloma eosinofilo osseo)
A. Crosta. *Radiologia Medica* [*Radiol. med., Torino*] **38**, 289–308, April, 1952. 10 figs., bibliography.

The author discusses the aetiology, pathology, differential diagnosis, treatment, and prognosis of eosinophilic granuloma; 3 personal cases are described and the radiographs reproduced.

Eosinophilic granuloma is a disease of the reticulo-endothelial system of children and young adults, more commonly occurring in males. The cause is unknown, though infection and trauma have been suspected, but it is now agreed by most workers to be an early stage of the reticulo-endotheliosis (Hans – Schüller – Christian syndrome and Letterer–Siewe's disease). If the disease process is confined to the first or eosinophilic phase the prognosis is good; but if it progresses to either of the other forms, then the prognosis becomes bad. Histologically, the basic cell is a large histiocyte or foam cell and not the eosinophil, which is merely a temporary and inessential feature. The bones affected are, in order of frequency, the skull, pelvis, ribs, vertebrae, mandible, long bones, and (rarely) short bones of the extremities. The lesions may be single or multiple, and the lungs, liver, and spleen may also be involved. The main symptoms are pain, tenderness and swelling of the affected part, and sometimes systemic upsets such as fever, loss of weight, and weakness.

The most important radiological features are single or multiple areas of destruction in one or more bones, with a smooth but irregular edge. In the long bones there is cortical involvement with little or no periosteal reaction; there is usually no expansion of the bone and there may or may not be sclerosis around the lesion; no generalized osteoporosis is present. In the skull the vault or base may be affected; suture lines are traversed and often the familiar " map-like " skull is seen. Laboratory investigations are nearly all negative and this helps to exclude a number of other conditions; a mild leucocytosis with a slight relative eosinophilia may be present. The diagnosis finally depends on biopsy, the histological findings being the most specific feature of the disease. Treatment is by surgery or radiotherapy, or both, and the results, especially in early cases, are very satisfactory.
E. L. Stein

1370. **The After-effects of Bronchography with Aqueous and Oily Contrast Media on Respiratory Function.** (Rilievi sulla funzionalità respiratoria in seguito a broncografia con mezzi di contrasto acquosi ed oleosi)
C. P. Curti and L. Donno. *Radiologia Medica* [*Radiol. med., Torino*] **38**, 364–369, April, 1952. 9 refs.

In order to determine whether bronchography, with either oily or aqueous contrast media, has any adverse effects on respiratory function, the authors examined a series of 9 patients immediately before bronchography and half an hour afterwards, while in 4 cases arterial oxygen and carbon dioxide estimations were repeated after 48 hours.

The following conclusions were reached concerning the effects of bronchography: (1) vital capacity is always reduced; (2) pulmonary ventilation becomes diminished; (3) respiratory dead space is reduced; and (4) there is increased mingling of arterial and venous blood. It was found that the results obtained half an hour after bronchography were similar whether oily or water-soluble contrast media were used. However, the oxygen saturation values obtained 48 hours later remained low when oily contrast medium had been used, but had returned to the initial level when a water-soluble medium had been used. *E. L. Stein*

1371. **Symptomless Circumscribed Intrathoracic Opacities: an Analysis of Fifty-six Consecutive Cases**
G. Cruickshank. *British Journal of Tuberculosis* [*Brit. J. Tuberc.*] **46**, 109–114, April, 1952. 7 figs., 1 ref.

An analysis is given of 52 cases in which radiographs showed round shadows in the lungs of symptomless patients. The *x*-ray diagnosis was confirmed at operation in 43 cases. The most important finding was that 8 patients were suffering from malignant disease and yet were completely free from symptoms. Pulmonary tuberculosis was found in 5 patients, and 5 others had diaphragmatic hernia, the correct diagnosis of which was made before operation either by a barium swallow or a diagnostic pneumoperitoneum. Other causes of

solitary round shadows in the lung included mesothelial cyst, mediastinal lipoma, silicotic nodule, extralobar sequestration, calcified haematoma, and hydatid cyst.

Kenneth Marsh

1372. **An Evaluation of Intracardiac Angiocardiography**
G. C. SUTTON, G. WENDEL, H. G. WEDELL, and D. C. SUTTON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **67**, 596–601, April, 1952. 9 refs.

The authors have compared two methods of angiocardiography: (1) by intracardiac catheterization; and (2) by the more usual technique of injection through a vein. The intracardiac technique was employed on 36 patients, all over 16 years of age, and the venous injection technique on 47.

The advantages of the direct procedure include high concentration of the opaque medium at the site of the investigation, and a clear field unobstructed by shadows of the medium in the right auricle and large veins. The dye can, if desired, be injected directly into the pulmonary artery. Accurate timing of the radiographs can be more easily achieved, and good films can be obtained with a relatively simple low-powered apparatus, the cassettes being hand-operated. The disadvantages are the slightly longer time required for carrying out the catheterization, the greater risk of reaction due to concentration of an irritant medium, and the risk of infection resulting from a slightly more elaborate surgical procedure. Transient arrhythmia was noticed in about one-third of the patients, and there was one death.

The results, which are tabulated, show that only in 3 of the 23 cases in which the angiocardiograms were not of diagnostic quality was intracardiac catheterization used. Of a further 23 cases giving a " useful, but less than desirable contrast " intracardiac catheterization was carried out in 10, and of the 37 in which good contrast films were obtained the catheter method was used in 23.

A. M. Rackow

1373. **Rapid Serial Angiography: Further Experience**
P. H. SCHURR and I. WICKBOM. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **15**, 110–118, May, 1952. 11 figs., 8 refs.

In 1949 Curtis published a report describing a method of rapid serial angiography of the cerebral vessels developed at the Radcliffe Infirmary, Oxford (*J. Neurol. Neurosurg. Psychiat.*, 1949, **12**, 167; *Abstracts of World Medicine*, 1950, **7**, 469). The present authors, who have continued his work, describe their findings in 109 serial angiographs taken from 74 patients.

Exposures were made on roll films, 10 inches (25 cm.) wide, moving between intensifying screens, frames being exposed at speeds up to 2 a second. Of the 109 angiographs, 21 showed no pathological condition. In these 21 cases there was marked variation in the cerebral circulation time, the venous phase varying from 2 seconds to $9\frac{1}{2}$ seconds and the arterial phase from $1\frac{1}{3}$ to $3\frac{1}{3}$ seconds. Much of this variation was technical, due to such factors as the speed of injection, amount and type of contrast material, and site of injection. Apart from these technical factors there was undoubtedly some physiological variation, due to changes in pulse and in blood pressure particularly.

With regard to the normal cerebral venous circulation, Curtis stated that the deep cerebral and certain superficial veins filled first and that the deep cerebral veins were the first to empty. This was not entirely confirmed; in 5 out of 20 normal cases the inferior longitudinal sinus filled first, and in 5 the deep cerebral veins emptied last.

The choroid plexus of the eye was seen as a " crescentic " line in 11 out of 20 normal cases; this was visible between 2 and $5\frac{1}{2}$ seconds.

Serial angiographs were particularly useful in selected pathological cases, for example, transient tumour filling was not overlooked and films at the optimum phase were obtained; in glioblastomata early venous filling in the tumour region was observed before the main cerebral veins were full; and in arterio-venous malformations the full extent of the lesion, with its afferent and efferent vessels, could be seen. In 2 cases thrombosis of the middle cerebral artery was seen, with retrograde filling of the middle cerebral vessels from the anterior cerebral.

The authors conclude that the method is useful in research and has an educational value in the interpretation of routine cerebral angiographs. *D. E. Fletcher*

1374. **Phlebography of the Vertebral Column and Skull by Intra-osseous Injections of Contrast Medium.** (Opacification des systèmes veineux rachidiens et craniens par voie osseuse)
H. FISCHGOLD, J. C. CLÉMENT, J. TALAIRACH, and J. ÉCOIEFFIER. *Presse Médicale* [*Pr. méd.*] **60**, 599–601, April 23, 1952. 4 figs., 12 refs.

The authors describe a method of phlebography of the vertebral column, in which they inject 50% diodone into one of the lower dorsal spinous processes. A brief description, with illustrations, of the external and internal vertebral venous plexuses thus outlined is given. For phlebography of the skull the patient lies in the prone position and 15 to 20 ml. of 50% diodone is injected into the external occipital protuberance. Lateral radiographs of the skull are taken towards the end of the injection and then at intervals of one second. Venous channels in three main directions are outlined by the contrast medium: (1) diploic vessels from the external occipital protuberance to the coronary suture and thence to the base of the skull; (2) the suboccipital venous plexus and posterior cervical veins; and (3) lateral sinuses and internal jugular veins. It was found that in the normal skull there was very little flow of diodone into the interior venous channels of the skull, but that the medium tended to collect in the outer soft tissues.

E. L. Stein

1375. **The Radiology of the Auditory Ossicles**
E. SAMUEL and G. THERON. *British Journal of Radiology* [*Brit. J. Radiol.*] **25**, 245–252, May, 1952. 17 figs., 4 refs.

In this paper from Johannesburg the authors point out that with the improvement in radiological equipment and technique the demonstration of the auditory ossicles

is now a practical proposition, and that the visualization of these bones is of great importance in planning treatment for various conditions that affect them.

They describe the normal anatomy of the ossicles, which is illustrated with radiographs of dissected specimens, and discuss the most favourable projections for their visualization. For the malleus and incus most information is obtained in the submento-vertical and Towne projections, but the former can also be seen in the lateral view. The stapes, which is the most difficult to visualize, is occasionally seen in routine views of the mastoid. They do not consider that tomography is of any help in the visualization of the ossicles. Attention is drawn to normal anatomical markings which may cause confusion, and it is pointed out that superimposition of the bony septa of the mastoid cells causes the greatest difficulty.

In a discussion of the different pathological conditions which may affect the auditory ossicles the authors suggest that the earliest radiological sign of neoplastic infiltration of the middle ear is absence of the ossicles.

W. B. D. Maile

1376. **Functional Radiodiagnosis with Radioactive Contrast Media.** (Funktionelle Strahlendiagnostik durch etikettierte Röntgenkontrastmittel)
H. Oeser and H. Billion. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **76**, 431–442, April, 1952. 11 figs.

A method of combined anatomical and functional study of the kidneys or of the gall-bladder and liver is described in which "uroselectan" or "biliselectan" labelled with radioactive iodine (^{131}I) is used in a dose of approximately 100 μc. Pyelography is carried out in the usual way but in addition the rate of excretion of the isotope is determined by comparing the radioactivity of periodic collections of urine with that of a standard preparation containing one-tenth of the dose of ^{131}I administered, the investigation being continued up to 36 hours following the administration. Similarly, following either intravenous or oral administration of radioactive biliselectan, radioactivity is measured over the region of the gall-bladder with a Geiger–Müller counter at regular intervals.

[For full details of this method of investigation the original paper should be consulted.] *A. Orley*

1377. **Nucleography**
P. R. Erlacher. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **34B**, 204–210, May, 1952. 12 figs.

Experiments with a watery solution of potassium iodide have shown that when injected into the nucleus pulposus the medium remains confined to the nuclear mass and to its extensions, if these have occurred. The author, writing from Vienna, considers that the use of nucleography is justified preoperatively for the precise location of herniations of the nucleus, and he is also of the opinion that the injection does not lead to herniation at the point of entry of the needle.

The author's technique of nucleography is carried out by means of a fine lumbar-puncture needle at least 12 cm. in length. The needle is inserted half an inch (1·25 cm.) lateral to and immediately above the level of the spinous process of the vertebra below the disk to be examined. It is directed upwards and medially (or downwards and medially in the case of the L5 disk) to reach the annulus fibrosus paradurally. When the elastic resistance of the annulus is felt, the needle is advanced 1·5 cm. Its position is checked by radiography in two planes before the opaque medium is injected. Only 1 to 2 ml. is required, the author using a 50% watery iodine medium ("ioduron"); for the L5 disk a 70% solution is used. Immediately after injection antero-posterior, lateral, and both oblique views are taken, the last with 15 degrees rotation of the patient.

In the normal case the nucleus appears as a globular shadow, or one showing a few large lobulations. In the abnormal case herniation or free prolapse may be found. Marked disk degeneration without prolapse is characterized by multiple branching with no central shadow. Two cases of prolapsed disk examined at the Wilhelminen Hospital, Vienna, are illustrated. *Kenneth A. Rowley*

1378. **The Radiological Features of Rheumatoid Arthritis**
D. E. Fletcher and K. A. Rowley. *British Journal of Radiology* [*Brit. J. Radiol.*] **25**, 282–295, June, 1952. 17 figs., 24 refs.

The clinical diagnosis of rheumatoid arthritis is fairly easy in the majority of cases, but the condition may be confused with subacute rheumatism, gout, Reynaud's disease, or polyarticular osteoarthritis. Generalized bone diseases, such as hyperparathyroidism and osteomalacia, have been mistaken for rheumatoid arthritis.

The authors, who have examined radiographs taken in 200 cases of rheumatoid arthritis at Manchester Royal Infirmary, found that the incidence of the disease was highest in the age group 40–50 years, with a sex ratio of 2 females to one male. In most cases there was radiological evidence of the disease within 3 to 6 months of onset. In general the changes seen radiologically were bone erosions; joint changes, consisting of alterations in width of the space, subluxation, and ankylosis; osteoporosis and so-called secondary osteoarthritis; and soft-tissue swellings. The incidence of local lesions was highest in the feet, especially in the 5th metatarsophalangeal joint, many enlarged radiographs showing an apparent splitting of the articular cortex and an irregular saw-toothed contour. The authors point out that exposure should be made for the region of the metatarsophalangeal joints and not for the foot as a whole. The authors' technique of enlargement is described. This is too involved for routine application but they recommend that for "the radiography of the extremities fine-grain industrial film should be used and processed for a reduced time in ordinary *x*-ray developer to obtain better detail".

[This informative article is well worth reading.]

Geo. Vilvandré

1379. **Arthrography**
K. Lindblom. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol.*] **3**, 151–163, Jan., 1952. 18 figs., 22 refs.

History of Medicine

1380. **Cotton Mather, the First Significant Figure in American Medicine**
O. T. BEALL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **26**, 103–116, March–April, 1952. 39 refs.

Cotton Mather is New England's most articulate representative of the tradition of clerical physician. Although his name is generally associated with the introduction of inoculation in the American colonies in the early 18th century, his writings show that he had a wide knowledge of medicine. He was the first writer in America to produce a general treatise on medicine and the first to demonstrate a knowledge of the animalcular theory of disease.

As a student at Harvard he was undecided whether to make medicine or the Church his career. When he finally chose the latter he retained his interest in medicine, although he subordinated it to religion; this is shown in his two earlier major works, the *Biblia Americana* and the *Magnalia*. The latter is the primary source of information for the historian of colonial medicine, because it cites many clergymen-physicians of the early period and notes the occurrence and distribution of disease. Mather's election to the Royal Society acted as a powerful stimulus to a renewal of his scientific interests. Between 1712 and 1724 he wrote nearly a hundred letters to the Society, and although they remain unpublished, many are medical documents and many others deal with the related subjects of philosophy, psychology, botany, and zoology.

Mather had a strong sense of duty in the field of public health, his leadership in this respect being evident during the epidemic of smallpox and measles which occurred in the first two decades of the 18th century. His fearless advocacy of inoculation in 1721 was only the culmination of many years of public health work.

Between 1720 and 1724 he was engaged in writing his large medical treatise, *The Angel of Bethesda*. It was never published, probably because the country was at that time beginning to frown on clergymen-physicians and Mather's prestige was, in consequence, not very high. The work lay unnoticed until 1869, when Dr. Oliver Wendell Holmes examined it, and his adverse criticism influenced all subsequent opinions of its worth. In the main he condemned the work as a terrible example of what happened when medicine was joined with religion.

Against a background of published medical writings by Americans, consisting only of pamphlets, *The Angel of Bethesda* is, however, unique in presenting an integrated system of medicine. It makes what appears to be the earliest statement in America of the animalcular theory of disease; and while showing the influence of ancient hypotheses and superstitions, it gives some account of the earliest medical practices in the New England colonies. The work deals with disease from both the religious and the practical point of view. The author considered that sin caused sickness, and therefore prayer rather than medication was his first concern for the sick. His practical theory of disease is basically Hippocratic in that it follows the classical view on humours and fluids; but clearly evident also is the influence on medical theory of certain discoveries of the 17th century. Mather's knowledge of the state of medical learning in Europe and his keen intellect enabled him to discover the weakest spot in the contemporary theory of disease —the lack of basic principles on which to erect a generally acceptable hypothesis. He preferred the iatromechanical concept of the human body, stating that diseases are the disorders of a machine, and that the physician must therefore be skilled in mathematics and mechanics and must understand the organization, structure, and operations of the machine-like body in order to regulate its defects and disorders.

The Angel of Bethesda illustrates " both the strengths and weaknesses of Mather's mind and of his age, and emphasizes the transitional character of both as they attempt to adjust themselves to the new discoveries in science ". Mather far outstripped such men as Boylston, Douglass, and Colden in the scope of his medical writings, and almost up to 1800 *The Angel of Bethesda* remained the only general medical treatise written in America. *Ruth Hodgkinson*

1381. **The Rise of Professional Surgery in the United States: 1800–1865**
C. R. HALL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **16**, 231–262, May–June, 1952. Bibliography.

1382. **A Student's Notebook of James Syme's Class of Clinical Surgery in 1861–62**
W. MCNEIL and C. MCNEIL. *Edinburgh Medical Journal* [*Edinb. med. J.*] **59**, 266–273, June, 1952. 2 figs.

1383. **The Mid-nineteenth Century Clinical School of Paris**
A. O. CAWADIAS. *Proceedings of the Royal Society o Medicine* [*Proc. roy. Soc. Med.*] **45**, 306–310, May, 1952.

1384. **Arabic Philosopher–Physicians and Christian Doctors of Medicine**
H. P. BAYON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **45**, 310–314, May, 1952. 3 refs.

1385. **The Dates of the Medical Renaissance. The End of the Traditions of Hippocrates and Galen.** (Les dates de la Renaissance médicale. Fin de la tradition hippocratique et galénique)
C. LICHTENTHAELER. *Gesnerus* [*Gesnerus*] **9**, 8–30, 1952. 22 refs.